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The aim of the present research is to equip our military leaders with knowledge and software tools which better assist them in the design of boot camp training regimens. More specifically, our research enhances of the state-of-the-art in bone overuse injury prediction. A significant part of our effort is geared towards the prediction and analysis of skeletal strain fields which result during a specific pattern of locomotion and for a given skeletal morphology. Once the intrinsic loads on the skeleton are known for various activities, it is possible to make educated inferences on how different training programs affect skeletal fatigue life, or in other words, the injury rate. First we researched and evaluated different approaches taken by others who have attempted to predict bone overuse injury rates before us. We then embarked on a multifaceted approach which utilizes biomechanics, inverse dynamics, static optimization, structural analysis, and statistical regression to determine skeletal fatigue loads during locomotion. The present deliverable is a model which accepts experimental video and force plate data gathered from normal gait as inputs and then determines the strain fields which arise due to the observed locomotion in a realistic simulated femur.

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Executive Summary

In the previous phase of the overuse injury assessment project, we developed a preliminary bone overuse injury prediction model based on the mechanisms of the injury and available field test data. However, the applicability of the model was severely limited by several factors. First, many parameters in the model could not be accurately estimated due to the lack of data or the lack of understanding of the underlying physical or biological process. Secondly, the stresses on the bone were approximated. Finally, the available field data were descriptive in nature and their relationship to the actual bone loading was not accurately established.

In this second year of the research project, we have focused our efforts on (1) reviewing the current status of bone overuse injury research, especially the mechanisms of injury, and methodologies such as predictive models, risk factors, and the diagnostic techniques; (2) better prediction of bone strains from laboratory tests using inverse dynamics, muscle dynamics, and finite element analysis; and (3) developing regression equations of gait parameters so that description training regimen can be quantified and the loads on the bone can be estimated.

Under repetitive loads and subsequently micro-damage accumulations, bone adapts both structurally (remodeling) and geometrically (modeling). Bone overuse injuries are the result of the imbalance between the damage accumulation and the repair, mostly caused by the increased physical activities during military training. The fundamental understanding of bone adaptation and failure, from the cellular level regulation of bone remodeling to its macroscopic quantification, is still preliminary and controversial. Yet it is generally accepted that bone strain is a fundamental variable to both the damage accumulation and the regulation of the bone adaptation.

We have undertaken a multifaceted approach drawing from a biomechanical modeling, inverse dynamics analysis, nonlinear optimization for muscle force, and structural analysis to accurately estimate bone strains from laboratory measurements of kinematics and ground reaction forces. For training data where these inputs not available, regression equations are established between different modes of locomotion and the gait parameters. These gait parameters can be accepted as inputs for biomechanical simulations.

Further review of the diagnostic methods of bone overuse injuries indicates that the current state-of-the-art technologies are time consuming, expensive and potentially dangerous. MRI is the gold-standard for detecting bone overuse injuries, being entirely safe and has the greatest diagnostic power. But it is also the most expensive diagnostic modality. In contrast, while emerging technologies such as ultrasound can be entirely safe, they have yet to be developed to a point where they are reliable indicators of a pathological bone condition.

Risk factor analysis is another commonly used method to determine which individuals and populations are most susceptible to bone injury. However, few such factors are widely recognized as being significant predictors of bone overuse injury. Conventional risk factor analysis based on demographics, personal history, anthropometrics and training errors is insufficient to gain real insight into the biological and biomechanical variations that separate those who are prone to bone overuse injury from those who are not. Models developed in this research, given enough laboratory data, may help to identify the real significant factors.

The future work will include collecting more laboratory and field data; formulating better methods for categorizing and quantifying training data; refining the biomechanical models to predict bone strains; and developing predictive tools that account for the inherent variation and uncertainty of field data. Such models predict bone strains which in turn can to provide a reasonable estimation of injury morbidity across a population.

1. Introduction

The aim of the present research is to equip our military leaders with knowledge and software tools which better assist them in the design of boot camp training regimens. More specifically, our research enhances of the state-of-the-art in bone overuse injury prediction. A significant part of our effort is geared towards the prediction and analysis of skeletal strain fields which result during a specific pattern of locomotion and for a given skeletal morphology. Once the intrinsic loads on the skeleton are known for various activities, it is possible to make educated inferences on how different training programs affect skeletal fatigue life, or in other words, the injury rate. First we researched and evaluated different approaches taken by others who have attempted to predict bone overuse injury rates before us. We then embarked on a multifaceted approach which utilizes biomechanics, inverse dynamics, static optimization, structural analysis, and statistical regression to determine skeletal fatigue loads during locomotion. The present deliverable is a model which accepts experimental video and force plate data gathered from normal gait as inputs and then determines the strain fields which arise due to the observed locomotion in a realistic simulated femur.

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2. Bone Strain, Damage, and Adaptation

2.1 Stress Fracture

A "stress fracture" is often not a frank fracture at all, but rather a pathological response of the body to an imposed fatigue strain on the bone. When the bone experiences a cyclic loading, the resulting strains in the bone inevitably generate a certain amount of microcracking (Lee, Mohsin et al. 2003). Compression-induced microcracking typically accumulates internally within the bone cortex, with most cracks running longitudinally along the interstitial bone (Boyce, Fyhrie et al. 1998). This accumulated damage is strongly correlated with a triggered regenerative response called remodeling (Lee, Mohsin et al. 2003). Damage is considered by many researchers to be the mechanism by which the body senses that remodeling needs to occur within the bone. However, this coincidence does not necessarily prove such causality. Other researchers have pointed to a different stimulus for remodeling associated with changes of blood flow within the bone (Otter, Qin et al. 1999). This is the reperfusion stimulus theory and will be discussed later in this chapter.

2.2 Bone Strain

Bones are subject to mechanical loads as a result of everyday use and normal locomotion. The mechanical loading of the lower extremities during locomotion is most easily resolved by gathering ground reaction force data in the laboratory. Each long bone in the legs can be considered to be loaded under a nominal axial stress which is defined as the axial force defined by the effective cross sectional area. Shear strains may also act within the plane of a bone cross section. But the most dangerous strains in the skeleton are typically bending strains which can result from the curved geometry of the long bones or joint torques. Bending strains are generally the greatest at the outer surfaces of the bone and may lead to structural failure in areas of tensile strain. Strains as high as 0.2 have been observed in humans during vigorous activity, which is about three times the strain observed during normal walking (Burr, Milgrom et al. 1996). These strains correlate to stresses of roughly 1 MPa during walking and 3-4 MPa during vigorous activity.

There are a number of methods engineers use to model and predict the fatigue lives of engineering materials. The most common means of representing the expected high-cycle fatigue life of a material is the S-N diagram which logarithmically plots the applied nominal stress against the observed number of cycles to failure. It has been observed that most materials have an endurance stress below which the number of cycles to failure is effectively infinite (i.e., greater than 10^6 cycles). For fatigue loads which vary with time or loading history, it is useful to apply Miner's Rule,

$$\sum \frac{n_i}{N_i} \geq 1,$$

where n_i is the number of cycles actually applied at a given stress level and N_i is the total number of cycles at that stress level which would lead to fatigue failure from a virgin state. A variety of cycle counting methods are available such as level-crossing counting, peak counting, simple range counting, and rainflow counting. These methods are described in more detail elsewhere (Bannatine, Comer et al. 1990). The fatigue stress in bone can be affected by a number of factors, including the overall bone geometry, the presence of defects, damage or other stress concentrators, as well as joint configuration and location of muscle insertions. Similarly, the fatigue life of bone undergoing a given fatigue load is affected by other intrinsic quantities such as the bone's internal quality, fracture toughness and even the condition of the bone surface, not to mention the effectiveness of biological regenerative mechanisms in living bone.

More vigorous locomotion tends results in greater skeletal strains. Similarly, long periods of locomotion contribute to skeletal fatigue. Increases in both intensity and duration of human movement result in an accelerated accumulation of damage in the bone and increases the probability of an overuse injury.

2.3 Damage Accumulation

Damage can be defined a number of different ways, depending on the material and the context in which it is studied. For the case of bone overuse injuries, microdamage is most accurately characterized as the amount of microcracking existing in the bone. Such microdamage can be subcategorized as cortical microcracks, diffuse damage, trabecular cross-hatched microcracking, and complete trabecular microfractures (Martin 2003). The different types of microdamage have been associated with different strain modes; tensile loading tends to produce diffuse microcracking while compressive loads tend to produce linear microcracks (Zioupos 2001). Microcracks have been observed to proliferate near microstructural strain concentrations in bone (Prendergast and Huiskes 1996). The presence of damage in bone has the effect of reducing its elastic modulus (Burr, Turner et al. 1998; Taylor 1998) as well as its fatigue resistance (Yeni and Fyhrie 2002) and fracture toughness (Zioupos 2001). For larger applied stresses, bone is observed to accumulate damage at a greater rate and fail more quickly (Carter and Caler 1985). Without a mechanism to remove microdamage which naturally accumulates in bone during physiological loading (Lee, Staines et al. 2002), the skeleton would fail much sooner than it does in vivo, or within the living organism (Taylor 1998).

2.4 Bone Adaptation to Fatigue Loads

2.4.1 Bone Modeling and Remodeling

Bone is a living tissue and it adapts its geometry and structure to the fatigue load conditions. On the microscopic scale, remodeling is thought to be controlled by networks of osteocytes (living bone cells) that exist in lacunae (small voids in the bone). Osteocytes may communicate with each other via canalicular channels. These pathways connect neighboring lacunae, possibly forming an interconnected three-dimensional network (Cowin and Moss 2001). Osteocyte lacunae are strain concentrators (Prendergast and Huiskes 1996) and are particularly suited for detection of imposed loads on the bone. Microdamage has also been observed to accumulate preferentially near osteocytes during fatigue loading of bone (Reilly 2000).

The cortex of the long bones of adults is mostly Haversian bone. Mature Haversian bone is largely composed of osteons, each of which is built like a thick lamellar straw (OD ≈ 100-200 μm) with a small blood vessel down the center. The process of remodeling—the renovation of this internal microstructure—is a two-step process involving osteoclasts (mobile bone destroying cells) and osteoblasts (mobile bone building cells). These cells form small teams called basic multicellular units (BMU's) which first excavate out damaged material from the bone, leaving osteon-sized holes in the material, and then fill them in with new bone material, leaving new osteons in their paths. The stationary osteocyte cells act as "mechanical engineers" which guide the "worker" BMU's to the damaged bone so that it can be replaced by new bone (Burger 2001). This process occurs over a period of weeks. In this framework, local strains, damage (microcracking), and/or changes in canalicular fluid pressure may be the stimulus which catalyzes remodeling.

Modeling—the addition of bone material to the periosteal (outer) or endosteal (inner) bone surfaces—is initiated by bone lining cells, which are actually flattened osteoblasts that reside on the quiescent bone surface (Jee 2001). When a greater bone mass is required, the bone lining cells awaken and act as osteoblasts, adding bone matrix to the outer and inner bone surfaces. When a lighter bone is required, the bone lining cells can become involved in osteoclastic resorption or may contract to allow other osteoclast cells to attack the bone surface. The biological process by which the need for a change in bone mass is sensed and bone lining cells are activated remains poorly understood.

If the loading stimulus is moderate, the remodeling response results in an overall strengthening of the bone such that it adapts to the new loading; that is, though bone is first removed by the BMU's, it is replaced quickly enough that the system adapts and stabilizes to the new loading. If the loading is too great, the accumulated loading creates a massive stimulus

for BMU activity and too many BMU's are activated at the same time. The BMU's then burrow out so much bone that it becomes pathologically soft and weak. In this way, the skeleton does everything possible to avoid the coalescence of microcracks into a macrocrack, even if it means substantially weakening itself in the process.

This condition (which may exist in the absence of a frank fracture) is what is often diagnosed as a "stress fracture" but is really more aptly termed as bone overuse injury. A description of different grades of bone overuse injuries is available (Zwas, Elkanovitch et al. 1987; Jones, Harris et al. 1989). The pain which results from bearing load on a bone which has undergone a pathogenic remodeling response to a large imposed loading is often too great to continue the loading such that a full fracture does occur.

2.4.2 Damage as a Stimulus for Remodeling

The prevalent thinking in the bone modeling community is that the rate of bone remodeling is affected by the amount of damage present in the bone. This assertion is supported by experimental observation of peaks of in vivo microdamage levels coinciding with peaks of remodeling activity (Lee, Staines et al. 2002). In fact, most experimental observations correlating fatigue microdamage and remodeling is circumstantial (Taylor and Lee 2003) and a direct causal relationship between bone damage accumulation and the acceleration of BMU activity has yet to be demonstrated. It has also been suggested that the fatigue microdamage hypothesis is not consistent with the typical bone overuse injuries observed in young people (Otter, Qin et al. 1999).

2.4.3 Ischemia/Reperfusion as Stimulus for Remodeling

The process of ischemia (starving of blood) and reperfusion (refilling with blood) has been shown to cause an increase in the remodeling rate in bone (Rubin, Gross et al. 1996). In particular, reperfusion has been linked to microvascular hemorrhaging due to the formation of damage in newly formed blood vessels of human bone grafts (Sckell, Demhartner et al. 2003). This condition may lead to osteocyte hypoxia (lack of oxygen) due to the interference of damage with canalicular nutrient flow. Hypoxia has also been linked to osteoclastic genesis (Arnett, Gibbons et al. 2003).

Ischemia and subsequent reperfusion has also been linked with the formation of hydrogen peroxide (Gasbarrini, Grigolo et al. 1997) which has been shown to cause osteocyte apoptosis (a programmed cell death by disintegration) (Kikuyama, Fukuda et al. 2002). Certain concentrations of hydrogen peroxide have also been linked with osteoclast formation and bone resorption in mice (Fraser, Helfrich et al. 1996).

It is therefore possible that damage causes osteonecrosis by a disruption of oxygenated blood supply to osteocytes through the canalicular networks (Tate, Tami et al. 2001; Tami, Nasser et al. 2002). The correlation between osteocyte apoptosis and local damage has been observed experimentally (Verborgt, Gibson et al. 2000). Hypoxia may also stimulate the activation of osteoclasts which resorb the dead bone. The implication of this hypothesis is that the accumulation of microdamage may only be one method of inducing remodeling in bone. Cyclic ischemia and reperfusion occurring in bone due to repetitive impact loading and changes in muscular blood requirements could have an even more direct effect on inducing a pathological remodeling response than microdamage during particularly intense bouts involving weight-bearing exercise.

2.5 Summary

The skeleton is the structural core of the body. Stress and strain concentrations occur within load bearing bones of humans during locomotion and other physical activities. The repetition of imposed fatigue loads—even those well below the maximum capacity of bones—can lead to the accumulation of microdamage in bone and an overall reduction of its structural capacity. However, since bone is a living tissue, it has the ability to adapt both microstructurally and morphologically to repetitive fatigue loads. Bone overuse injuries are thought to be the result of an imbalance between skeletal damage accumulation and repair. But the scientific community's fundamental understanding of how the skeleton responds to fatigue—from the level of bone cells up to that of entire bones—remains incomplete. At least it is agreed that stress and strain are a variables which are fundamental in both causing damage accumulation and bone's ability to direct regeneration. While it is difficult to predict bone overuse injuries accurately on an individual basis without a better understanding of underlying biological processes involved, it is feasible to predict the injury rates for a population undergoing a certain training program. Such a predictive undertaking requires the accurate analysis of bone strains for different activities. This, in turn, depends upon sufficient experimental data being available to enable the establishment of meaningful correlations between strains in bone and bone overuse injuries.

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3. State-of-the-Art Predictive Models

3.1 Physics-based Predictive Models

One approach to the prediction of bone overuse injury is the employment of a physics-based model. Physics-based relations tend to by nature be more complex than simpler phenomenological models since they use mathematics to describe physical processes going on in a material or organism. In the constitutive modeling of metals, a physics-based model would have mathematical relations which describe the formation of geometrically necessary dislocations and statistical dislocations, plasticity via dislocation glide, the hardening of the metal through the entanglement of previously mobile dislocations, the formation of dislocation networks through climb and glide processes, as well as thermal recovery and annihilation of mobile dislocations. The Martin model, described in a following section, is a good example of a largely physics-based model; though some of the relations used to describe the physical processes are empirically-derived (such as the relationship between applied strain range and damage accumulation) the overall model is designed to simulate actual biological processes. Similarly, the Taylor model, also described below, is partly physics-based in that it describes the evolution of microstructural cracks in bone. But the Taylor model is quintessentially an empirical model since the crack growth relations used are entirely phenomenological. While physics-based models do not often enjoy the same predictive power enjoyed by empirical relations, they have the benefit of each component having physical meaning. This allows for better analysis of the simulation data; that is, the evolution of the components of physics-based models can be examined to infer information about the system being modeled which might otherwise be unattainable experimentally.

The highly complex ways in which living bone adapts to an environmental loading makes the application of conventional theories used to describe the fatigue of engineering materials to bone questionable. By most clinical observations, the diagnosis of a bone "stress fracture" has in fact little to do with the formation of any kind of observable fracture in the bone. During periods of abruptly increased activity, the time to diagnosis of a symptomatic, clinically diagnosable bone overuse injury is far shorter than is predicted for comparable fatigue loadings of dead bone in vitro (or "ex vivo" meaning artificially, outside the living organism). For in vitro models a critical crack length or drop in modulus is used as the criterion for injury occurance (Martin 2001).

It has been suggested (Taylor, O'Brien et al. 1999) that a statistical size effect may account for the discrepancy between fatigue lives observed in vivo and in vitro. While this theory may account for some of this discrepancy in tibial overuse injuries (i.e., when the full bone loaded in vivo is significantly longer than the bone specimens tested in vitro, or outside of the living

organism), it does not account for the early injury which occurs in smaller bones, such as the metatarsus and navicular of the feet, which are of similar size to specimens tested in vitro.

The formation of microcracks may play a role in the formation of bone overuse injuries, but it does not appear that overuse injuries in bone are the direct result of an excessive accumulation of fatigue damage. Arguments for an indirect causality are more convincing. Instead, the quintessential processes which drive such injuries appears to be the very same remodeling processes which have arisen as a means of rejuvenating bone and recovering microdamage. Two complimentary approaches to modeling bone overuse injuries are now discussed.

3.1.1 The Taylor Model

The Taylor model (Taylor and Lee 2003) simulates the evolution of a microcrack up to a full skeletal fracture. The growth of a crack of length a over a number of cycles N is given by the empirical relation

$$\frac{da}{dN} = C'(\Delta K)^{n'}\left(\frac{d-a}{d}\right)^{m} + C(\Delta K - \Delta K_{th})^{n}, \quad \Delta K = F\Delta\sigma\sqrt{\pi a},$$

where C, C', n, n' and ΔK_{th} are phenomenological material constants and F and d are parameters describing crack geometry and microstructural spacing in the direction of crack growth. The first term describes the growth of a microstructurally short crack as it decelerates towards a crack length d. The second term describes the unstable growth of a microstructurally large crack. Either term is set to zero if it becomes negative.

Remodeling in this theory is related to a shortening of this crack and is always a process which strengthens the bone. In reality, this is an unlikely relationship since the short crack growth theory predicts that the majority of the fatigue life of a crack is spent when it is microstructurally short (< 100 μm); most crack-annihilating BMU's are 100 μm or more in diameter. Therefore, the recovery of a population of microcracks via BMU remodeling activity is more likely a case of short crack elimination than crack shortening.

The use of scintigraphy and MRI to visualize bone overuse injuries in vivo has revealed bone overuse injuries tend to form well before any cracks are resolvable radiologically. Bone injuries are sometimes detectable even before any symptoms are presented (Zwas, Elkanovitch et al. 1987). This makes the underlying physical assumptions of the Taylor model (that crack length is a predictor of bone overuse injury) questionable. While actual fractures are sometimes observed within the scintigraphic hot spot associated with a bone overuse injury, it only does so in the higher grades injury after the initial symptoms such as pain have been ignored and fatigue loading has continued. As such, the Taylor model does not appear to be designed to

describe the physical phenomenon which leads initially to the bone overuse injuries experienced by most active people and soldiers; that is, a pathogenic remodeling response to fatigue strains.

3.1.2 The Martin Model

In contrast, the Martin model (Martin 2001) describes microcracking using a damage parameter which is defined as the sum of all crack lengths over a given area. Damage accumulation is related to the fatigue loading,

$$\dot{D}_F = k_D R_L \varepsilon^q,$$

where k_D and q are material constants, R_L is the loading rate and ε is the strain range.

The Martin theory diverges fundamentally from the Taylor approach in that the biological processes contributing to remodeling in the Martin model can be either beneficial or pathological. Martin uses his model to illustrate how the process of remodeling may fall into a "good loop" or "bad loop" depending on the loading level (Martin 2001). In the good loop, remodeling results in damage removal and attainment of a new bone geometry which compensates for increases in external loading. The bad loop occurs when the loading stimulus is so substantial that remodeling causes the bone porosity to increase to a point where an overuse injury occurs. The rate of remodeling is assumed to be driven by the accumulation of damage,

$$\dot{D}_R = D f_a A_o F_S,$$

where $\dot{D}_R$ is the rate of damage removal, D is the current damage, A_o is the area excavated out by a BMU on a transverse cross section, F_S is a material constant and f_a relates damage and remodeling by

$$f_a = \frac{f_{a\max} f_{a\min}}{f_{a\min} + (f_{a\min} - f_{a\min}) \exp\left[-k_R f_{a\max}\left(\frac{D - D_o}{D_o}\right)\right]},$$

which is a sigmoidal relationship bounded by the values $f_{a\min}$ and $f_{a\max}$. The Martin model accounts for reduction in modulus due to increased bone porosity associated with increased remodeling activity over a time step i using the relation

$$P_i = P_{i-1} + \left(N_R Q_R - N_F Q_F\right)\Delta t\,,$$

where N is the number of BMU's acting on a given bone cross section, Q is the rate change of bone area in the cross section due to BMU activity and the subscripts R and F stand for resorbing (subtracting) and filling (adding) bone, respectively. The modulus is then related to the porosity by

$$E = \left(20.0\text{ GPa}\right)\left(1 - P^3\right)$$

and the bone strain resulting from an applied stress is then given by a simple Hooke's Law

$$\varepsilon = \frac{\sigma}{E}.$$

Once the bone strain reaches a critical value associated with in vitro fracture failure, a bone overuse injury is said to have occurred. Despite its association with an in vitro fracture mode, the failure strain is not a sensitive parameter since the model becomes unstable quickly once the simulated remodeling becomes pathological. In addition to remodeling, the bone is also simulated to perform surface modeling when increased fatigue loads result in greater damage accumulation:

$$M_P = k_P\left(D - D_C\right),$$

where M_P is the surface apposition (growth) rate and D_C and k_P are material constants.

The Martin model describes the underlying biological processes believed to lead to bone overuse injuries, but lacks predictive power because some critical relations are estimates, such as the mathematical relationship between damage accumulation, D, and BMU activity, f_a. Many of the parameters are not well defined by experimental observation. Of particular concern is a damage growth exponent, q, which has been found experimentally to vary over an order of magnitude. As a result, the model can predict vastly different fatigue lives depending on what value is used. While this model has perhaps the greatest potential of those reviewed in the literature, the state of knowledge does not appear to be mature enough to support the employment of this model in a predictive fashion. Martin admits that the model, in its current state, is not meant to be quantitatively predictive, but rather is illustrative of his theory regarding the relationship between bone damage and remodeling (Martin 2001).

3.1.3 A Hybrid Model

While it is possible that a hybrid Taylor-Martin model could result in more accurate prediction, it should be understood that the underlying models are founded in fundamentally different views of what a bone overuse injury is and what the processes are that cause it. In particular, the strength of the Taylor model is its description of the evolution of a population of microcracks undergoing fatigue loading. This strength does not assist in the predictive framework of the Martin model where microcracks (Martin's "damage") are assumed to not have a chance to grow significantly before they are either removed or a pathological remodeling response occurs.

In addition, the Taylor model employs the common assumption that a population of microcracks forms on the first cycle of loading according to the relation

$$\rho_v = A(\sigma_{\max})^b,$$

where ρ_v is the density of microcracks, $\sigma_{\max}$ is the maximum stress attained in the first cycle and A and b are constants (Taylor and Lee 2003). Note that this power-law relation is similar to the power-law relation Martin uses to predict damage accumulation from the applied strain range. (Remember elastic strains are directly related to stresses in Hooke's Law.) In fact, the Taylor model sensitivity to the exponent b will be similar to that for the Martin model exponent q. This is because the Taylor model exhibits sensitivity to the initial crack length, particularly if the longest cracks initiated are of comparable size to the microstructural parameter d. Assuming a Weibull (or similar) distribution of initial microcrack lengths, the more times that this distribution is sampled; that is, the higher the value of ρ_v, the greater the probability that a particularly large crack will be chosen. The growth of cracks is deterministic in the Taylor model, so it is the largest crack which will control the time to failure. For a given distribution of crack sizes, the longest initial crack length is sensitive to the exponent b; small variations in this parameter could also strongly affect the predicted fatigue life of the bone. Therefore, in addition to an uncertain physical underpinning, the application of the Taylor model may suffer from the same instabilities associated with material parameter uncertainties that the Martin model does. Neither of these models is suitable in its current state for accurate prediction of bone overuse injuries in individuals or populations.

3.1.4 Biological Relations and Parameters

Even if there was an adequately designed material model for living bone—complete with accurate material and biological parameters—it is unlikely that such a model could be employed in a predictive fashion in a boot camp or for an athletic team in the foreseeable future. Most of the inputs required for a physics-based model (such as that relating fatigue loading to

BMU activity in a given individual) are expensive, difficult, or impossible to obtain clinically. As such, the response of entire populations to a given training plan might be possible to predict given some room for error, but the prediction of an individual's response to different loads will be unreliable without an accurate set of material and biological constants determined for that individual. As we will review in a later section, the current state-of-the-art diagnostic modalities are unable to provide all of the requisite information to make such a prediction possible.

3.2 Phenomenological Models

3.2.1 Empirical Models

Empirical relations can be thought of as regression relations that are simply fit to experimental data provided. The constants used do not necessarily have a physical meaning and the governing equations are not restricted to be dimensionally homogeneous. On average, empirical relations tend to have a great predictive power, as long as the application of the calibrated model fits within the domain of the data collected. In other words, empirical relations become dangerously unpredictable when they extrapolate outside of the scope calibration dataset. Empirical models tend to be the simplest, most robust, easiest to calibrate and most computationally inexpensive of material models.

3.2.2 Neural Networks

Neural networks can be employed when large data sets are available and all that is desired is the prediction of future events based on interpolation of the data collected. In this context, based on a database comparing background history and anthropometric data of a large number of Marine recruits to incidence of fatigue-related bone injury, a neural network could be a powerful predictive tool for predicting incidence of bone overuse injury based on such data in future recruits. However, the neural network should be seen as a "black box" as it is a simple pattern recognition filter which provides no information as to its inner workings. In addition, the predictive power of a neural network is only as powerful as its training set permits. Larger training sets tend to result in greater predictive capabilities; however, if the data set does not include all variables which are of predictive importance (i.e., a critical risk factor for bone overuse injury is not sampled), the predictions made will be unreliable. Also, while neural networks are useful for interpolating over the domain of the training data, they should not be applied to extrapolate outside of the domain of the training data. For instance, if the largest individual included in the Marine recruit training data set described earlier was 100 kg, then the neural network would be unreliable in predicting the time to failure for recruits larger than this size. Therefore, while the neural network approach to predicting bone overuse injury is enticing

in its brute force approach, it should be considered with healthy skepticism as a long-term solution to the problem.

3.3 Review of Modeling Approaches

3.3.1 Complexity

Once a model type has been chosen and accurately formulated, it must be calibrated for the predictive task at hand through the determination of associated material constants. The constants for an empirical model should, by design, be relatively easy to obtain. But some constants, such as exponents, may be sensitive to variation and may require a large data set to obtain with sufficient accuracy. The constants can be relatively easy to attain (such as those determined from body mass, total height, or past physical training) or more difficult to attain (such as those describing internal biological processes).

Regardless of the nature of the model constants employed, the following rule of thumb holds: While adding complexity to a predictive model via additional material parameters will expand its ability to capture different phenomena and behaviors, each new parameter added retains a degree of uncertainty in its measurement and this uncertainty detracts from the model's predictive power. Therefore, the most robust predictive models contain the minimum amount of complexity. This is the predictive advantage empirical models have over physics-based models. Physics-based models, almost by definition, contain a large number of physical, biological and material constants, as compared to empirical models. This is why the Martin model, despite its apparently sound biological underpinnings, is not yet ready to be employed in a quantitatively predictive fashion.

3.3.2 Data Sets

In order for an empirical model or neural network to be successful in predicting the occurrence of bone overuse injuries in a population, it is important to first gather a large data set from which it is possible to determine the mathematical form of the empirical relation and associated material constants for the empirical model or use as training data for a neural network. While some studies involving thousands of subjects have been performed, the relatively low occurrence of bone overuse injuries during of these studies makes the data collected insufficient for reliably defining parameters for an empirical model or neural network. In order to collect such a data set for military recruits, procedures which take periodic and comprehensive measurements of recruit history, anthropometric and injury data would need to be put in place. We do not anticipate that such an approach would be received well in the military.

For a purely physics-based model to be successful, a somewhat smaller data set could be used for calibration of the model, but even more extensive diagnostic techniques would need to be developed and employed. Such diagnostic techniques would take measurements in vivo which could help in determining constants relating microscopic and biological processes of bone damage, modeling and remodeling such as those described previously. Progress is being made on such research using animal subjects which are to be killed and examined post mortem, but progress has been slower in research on human subjects where such procedures tend to be discouraged. The development of new methods to look more deeply, more microscopically, and less destructively into the human body, is needed to enhance the predictive power of physics-based bone overuse injury models as well as our understanding of this phenomenon.

3.3.3 The Current State of Knowledge

The fundamental understanding of bone modeling, remodeling and the formation of bone overuse injuries is yet embryonic. At the 12th Conference of the European Society of Biomechanics (August 2000), a list was generated of research topics in most need of fundamental research, along with a priority score of 1-4 (Prendergast and McCormack 2002). Relevant highlights follow:

- To determine the relationship to mechano-regulation and cell metabolism in osteoporosis (#4, priority = 3.56)
- To quantify the mechanical loading of the skeleton in vivo (#7, priority = 3.51)
- To develop a method to quantify bone micro-damage clinically (#8, priority = 3.48)
- To determine the mechanical stimuli for maintenance of bone quality in human activity (#12, priority = 3.43)
- To treat tissue microdamage and prevent damage fracture (#13, priority = 3.40)
- To determine if damage signals bone remodeling (#14, priority = 3.38)
- To determine the relationship between damage and microstructure in bone (#17, priority = 3.27)

The items in this list indicate that an improvement is needed in the fundamental understanding of how bones adapt and fail. Without such requisite fundamental knowledge of the phenomena involved leading to bone overuse injuries in place, the formation of a useful physics-based predictive model is unlikely.

Assuming that a pathological remodeling response of the bone to a mechanical overload is the cause of bone overuse injuries—as opposed to a stress fracture being a form of frank fracture—then predictive modeling efforts along this line are further complicated. While prediction of the evolution of microdamage in bone is subject to a certain variation of physical

factors (e.g., the exact distribution of microcrack size and orientation and relevant microstructural spacing in the bone of a given individual), the prediction of the remodeling response is also subject to variation of biological parameters from one individual to the next (e.g., the relationship between fatigue loading and BMU activity and the respective rates of BMU bone resorption and refilling for a given individual). Such additional biological variations complicate efforts to predict bone overuse injury in models which are not designed to account for these variations.

One method currently employed, in an attempt to identify individuals or populations who are prone to such bone overuse injuries prior to training, is risk factors analysis. A notable amount of work has been done in this area already (Giladi, Milgrom et al. 1987; Giladi, Milgrom et al. 1991; Milgrom, Finestone et al. 1994; Lappe, Stegman et al. 2001). Other research has examined the commonalities in activities within a set of injury prone individuals. Such information could potentially be useful in designing alternate training arrangements which minimize the time and money lost to injury in boot camp. There has been some notable research in this area as well (Milgrom 1989; Milgrom, Finestone et al. 2000; Milgrom, Simkin et al. 2000) though few recommendations stemming from this approach have been widely accepted. A summary of risk factors for bone overuse injury that has been published in the literature is presented later in the chapter.

3.3.4 Remaining Questions

It is important to accurately characterize an individual's biological response to loading if a reliable in vivo skeletal fatigue life prediction is to be made. Diagnostic modalities currently available have yet to answer a set of basic, yet difficult questions and do it in a safe, fast and cost-effective fashion:

- What is the relationship between the intrinsic fatigue loading of the skeleton and the BMU activation rate?
- Once osteoclastic resorption is activated at a given rate, how quickly does the bone weaken?
- Once osteoclastic resorption weakens the bone, how quickly does osteoblastic deposition restore the bone's load bearing capacity?
- Taking modeling and remodeling into account, at what intrinsic critical strain or number of fatigue cycles at a given intrinsic load do we expect a frank fracture to occur?

The utilization of current advanced bone injury diagnostic modalities such as MRI and bone scintigram during examinations is another way of minimizing time lost to such injuries by

catching them before they become severe (as opposed to making a long term prediction). Once the early stages of a bone overuse injury are detected, the affected individual could be put on a modified training plan which allows for recovery. The diagnostic modalities currently available are now reviewed.

3.4 Diagnostic Modalities

3.4.1 Radiography (X-rays)

- Most ubiquitous technology and often used first, but is relatively insensitive to bone overuse injuries.
- Low risk; however, the risk increases as numerous additional radiographs are performed.
- Results typically read negative for up to 3 months after the initial injury or may never resolve the injury.
- Overall false negative rate = 0.50.
- Incapable of detecting diseased tendon and soft tissue malignancies.
- Resolution: ~0.5mm.

3.4.2 Dual Energy X-ray Absorptiometry (DXA)

- Evaluates how much energy is absorbed by bone from x-rays at two different energies.
- Used to characterize bone cross sectional area, bone mineral density (BMD).
- Currently the preferred method for measuring BMD.
- Can capture the entire skeleton on one image.
- Negligible radiation (entrance exposure of less than 5 mR, one tenth of CAT scans).
- Resolution: ~0.5mm.

3.4.3 Computed Tomography (CT/CAT)

- Utilizes x-rays to generate serial sections of the body.
- Low risk; however, the risk increases as numerous additional scans are performed.
- Resolution: ~1-2mm.
- False negative rate high compared to BS or MRI.

3.4.4 *Bone Scintigraphy (BS/Bone scan)*

- Uses a gamma camera (of similar penetration as a diagnostic x-ray beam) and injected Technetium 99m diphosphonate or polyphosphonate radioactive tracer in the blood (half life ~6 hrs) to observe bone quality in three phases:
  - Phase 1: (immediately after injection) shows increased tracer perfusion in the area of the bone overuse injury.
  - Phase 2: (1 minute after injection) shows degree of hyperemia (engorgement) and local capillary permeability of bone.
  - Phase 3: (3-4 hours after injection) shows preferential tracer pooling in the area of the injury.
- Highly effective at early diagnosis of overuse injuries in long bones such as the tibia and femur. Reads positive within 6 to 72 hours after initial injury.
- Can capture the entire skeleton on one image.
- The patient is exposed to radioactive material though many consider the radiation exposure negligible (entrance exposure of less than 5 mR).
- False negatives are rarely reported (Milgrom, Chisin et al. 1984) and normal bone scan reliably excludes the diagnosis of bone overuse injury (Zwas, Elkanovitch et al. 1987), though false positives have been reported (Shin, Morin et al. 1996).
- Currently the gold standard for the detection of some kind of pathological bone condition.
- BS lacks specificity (Shin, Morin et al. 1996). For cases where a pathological condition is revealed in the bone, it may be difficult to determine the exact cause of the pathology. The diagnosis of the condition can have a strong influence on the plan of treatment.
- BS may read positive for up to 12 months after initial injury.
- Resolution: ~1mm.
- Single (or Dual) Photon Emission Computed Tomography (SPECT) uses a gamma camera to diagnose conditions in bones of more complex geometry, such as the pelvis and spinal vertebrae.

3.4.5 *Magnetic Resonance Imaging (MRI)*

- Utilizes the knowledge that nuclear magnetic relaxation times after the application of a magnetic field differs for different tissues.
- Has a higher spatial resolution than BS or CAT.

- Has the capability of detecting other malignancies in the bone which would make it prone to insufficiency fracture.
- Becoming the gold standard for the diagnosis of bone overuse injuries. The determination of the nature of injury or condition may affect the plan of treatment.
- Is reported to have 100% sensitivity (true positives and negatives), specificity, and accuracy (Shin, Morin et al. 1996).
- Does not image cortical bone as well as CAT scans.
- Resolution: ~0.5mm
- Safe.
- False positive/negative rate is low.

3.4.6 *Undeveloped Diagnostic Modalities*

Quantitative Ultrasound (QUS)

- Uses speed of sound (SOS) and broadband ultrasound attenuation (BUA) to characterize bone condition in the cortex and trabeculae.
- QUS diagnostic devices typically operate at an intensity that is nonheating (5-50 mW/cm^2) which is of similar intensity as that used in US imaging of unborn infants and should not be confused with the intensities used for therapeutic US (50 W/cm^2).
- QUS methods are already USDA approved and are totally safe.
- Commercially-available QUS devices designed for diagnosing risk of osteoporotic fracture are relatively portable (10 kg) and can be operated by a clinician.
- These units have been shown to be able to discriminate between populations which have suffered osteoporotic fracture from those who have not by analyzing a site (the calcaneous, or heel bone) which is not directly associated with the fracture.
- The use of higher-intensity ultrasound (2 W/cm^2) to elicit pain selectively in bone injuries has been found to be a poor predictor for bone overuse injury in individuals (sensitivity: 43%, specificity: 49%, positive predictive value: 41%, negative predictive value: 51%) when using BS as a standard of measurement (Devereaux, Parr et al. 1984; Boam, Miser et al. 1996).

Imaging Ultrasound (US)

- In contrast to QUS, where the wave is transmitted through the bone, US imaging uses sonography to observe different regions under the skin.

- State-of-the-art ultrasound imaging devices see bone as a hyperechoic material and are not able to resolve internal bone structure or condition.
- US has the potential for use as tool for characterizing external bone geometry for biomechanical analysis.
- Some research has been able to use sonographic US techniques to characterize cortical bone thickness by examining the US signal reflected from the endosteal surface of the cortex as well as the initial reflection from the periosteum (Wear 2003).
- Other research has found US imaging to be more sensitive than MRI for the detection of soft tissue injuries of the elbow (Popovic, Ferrara et al. 2001).

Thermography

- Uses infrared light to create a skin surface temperature image map. The warmer regions of skin are thought to correlate to bone overuse injury.
- (McBryde 1985): "Thermography can detect stress changes in bone easily and within hours of clinical symptoms."
- Thermography has 80% sensitivity for bone overuse injuries, using BS as a control (Devereaux, Parr et al. 1984).

Vibration

- The determination of resonant frequencies (~130 Hz) of different bone specimens using applied vibration has been tested as a means of determining overall bone quality. It was determined that resonant measurements which do not account for mass and length of the bone are unable to determine bone quality, but it was suggested that this should be possible with reliable measures of bone mass and length (Van Der Perre and Lowet 1996).
- A more recent published review of vibration techniques used clinically expressed concern whether vibration diagnostic methods would ever be reliable due to problems with soft tissue and interpretation of results (Nokes 1999). It was noted that many who did research on the use of vibration as a diagnostic modality have shifted their research focus to ultrasonic techniques.

3.4.7 Diagnostics Outlook

Most of the state-of-the-art bone diagnostic modalities for use in the detection and diagnosis of bone overuse injuries tend to be time consuming (lasting from about 30 minutes to hours), expensive (ranging from $100's to $1000's per individual use and requiring a dedicated technical staff) and potentially dangerous (e.g., exposure to x-rays or radiological material). Of

the above technologies, MRI is becoming recognized as the best modality for diagnosing bone overuse injuries, being entirely safe and having the greatest diagnostic power. However, this modality is also the most expensive and will not be widely applied in routine preventive exams for the foreseeable future.

A few of the emerging diagnostic modalities listed above show some potential for predicting and diagnosing bone overuse injuries in the clinical setting. In particular, the use of ultrasonic technologies for both imaging and bone quality characterization is slowly moving from the fringes of medicine to the mainstream as this technology becomes more sophisticated, accurate, and reliable. In fact, all three of the embryonic technologies listed above share the property of being totally safe and noninvasive as well as the potential to be cheap and portable. This limits the danger of applying these modalities although there is always a potential for arriving at a false-negative diagnosis. Further research exploring the developmental potential of these technologies could lead to a new, more versatile, more cost effective means of reducing bone overuse mobility in military and athletic individuals.

3.5 Risk Factors for Bone Overuse Injuries

A popular approach to predicting bone overuse injuries in individuals and populations is through identification of certain risk factors. The data used to identify risk factors is gathered through studies of individuals and populations. Such investigations range from prospective studies (the population studied is identified prior to exposure) to retrospective studies (the population studied is identified after exposure has already occurred) to case studies (retrospective investigations of individuals) and the set of anthropometric and aetiological parameters studied varies from one investigation to the next. Risk factors are attained by the determination of which variables have a statistically significant correlation to the bone overuse injury morbidity for a given study. Below is a listing of risk factors published in the literature, grouped by type.

3.5.1 Demographic Risk Factors

- Age, with a positive correlation with injury rate (Brudvig, Gudger et al. 1983; Lappe, Stegman et al. 2001), negative correlation (Milgrom, Finestone et al. 1994; Winfield, Moore et al. 1997) or no correlation (Reinker and Ozburne 1979; Brunet, Cook et al. 1990; Ross and Woodward 1994; Shaffer, Brodine et al. 1999)
- Race, with whites more susceptible than blacks (Brudvig, Gudger et al. 1983; Gardner, Dziados et al. 1988; Milgrom, Finestone et al. 1994), while others found no correlation (Winfield, Moore et al. 1997; Shaffer, Brodine et al. 1999)

- Sex, with females more susceptible than males in military populations (Protzman and Griffis 1977; Reinker and Ozburne 1979; Brudvig, Gudger et al. 1983; Hulkko and Orava 1987; Jones, Harris et al. 1989; Brunet, Cook et al. 1990; Ross and Woodward 1994; Fredericson, Bergman et al. 1995); however, this is not seen in athletic populations (Bennell, Malcolm et al. 1996; Bennell and Brukner 1997), suggesting that there may be an initial difference between the sexes in a different risk factor—such as initial fitness level—in military recruits.

3.5.2 *Personal History Risk Factors*

- Initial fitness level (Kowal 1980; Greaney, Gerber et al. 1983; Gardner, Dziados et al. 1988; Ross and Woodward 1994; Shaffer, Brodine et al. 1999) or running more prior to training (Macera, Pate et al. 1989; Montgomery, Nelson et al. 1989; Shwayhat, Linenger et al. 1994; Winfield, Moore et al. 1997), although no correlation to injury has also been found (Mustajoki, Laapio et al. 1983; Milgrom, Giladi et al. 1986; Myburgh, Grobler et al. 1988; Zahger, Abramovitz et al. 1988; Swissa, Milgrom et al. 1989; Giladi, Milgrom et al. 1991; Hoffman, Chapnik et al. 1999).
- Low calcium intake for females (Myburgh, Grobler et al. 1988; Myburgh, Hutchins et al. 1990), though others have found no correlation between the calcium metabolism and injury for males (Mustajoki, Laapio et al. 1983) or any such correlation for self-reporting of dairy intake for females (Lappe, Stegman et al. 2001).
- Age of menarche or first menstruation (Carbon, Sambrook et al. 1990; Bennell, Malcolm et al. 1996) though others have found no correlation to injury (Myburgh, Hutchins et al. 1990).
- Lowest previous adult body weight (Lappe, Stegman et al. 2001). One hypothesis explaining low current body weight as a risk factor is that all recruits are forced to carry equal weight packs, regardless of their current size. This additional load is a greater percent increase for smaller recruits who will be naturally adapted to carrying only their normal body weight (Beck, Ruff et al. 1996). One way to potentially reduce the incidence of bone overuse injuries is to have the maximum pack weight during training scaled by the initial weight or lowest adult weight of the recruit.
- Use of birth control patch (Lappe, Stegman et al. 2001) or no correlation of birth control use and injury (Winfield, Moore et al. 1997)
- Alcohol or tobacco use (Altarac, Gardner et al. 2000; Lappe, Stegman et al. 2001) though others report no correlation with injury (Ross and Woodward 1994; Shaffer, Brodine et al. 1999).

- Previous bone overuse injury (Milgrom, Giladi et al. 1985; Macera, Pate et al. 1989; Crossley, Bennell et al. 1999; Hootman, Macera et al. 2002)
- Lower BMD in males (Beck, Ruff et al. 1996), high BMD in males (Crossley, Bennell et al. 1999) and still others have found no correlation with injury (Giladi, Milgrom et al. 1991; Crossley, Bennell et al. 1999).
- Lower BMD in females (Myburgh, Hutchins et al. 1990; Brukner, Bradshaw et al. 1996), amenorrhea (not menstruating) (Myburgh, Bachrach et al. 1993; Anderson and Greenspan 1996; Brukner, Bradshaw et al. 1996) and menstrual irregularities (Carbon, Sambrook et al. 1990; Winfield, Moore et al. 1997; Korpelainen, Orava et al. 2001). Low BMD is seen in amenorrheic women when compared to eumenorrheic (normally menstruating) peers (Drinkwater, Nilson et al. 1984; Myburgh, Bachrach et al. 1993). Other research has found no correlation between menstrual status and bone overuse injury risk (Myburgh, Grobler et al. 1988; Grimston, Engsberg et al. 1990).

3.5.3 *Biomechanical Risk Factors*

- Low current body weight (Beck, Ruff et al. 1996) high current body weight, in females (Kowal 1980) or no correlation with injury (Reinker and Ozburne 1979).
- Less lean mass in the legs in females (Brukner, Bradshaw et al. 1996).
- Overall shortness (Beck, Ruff et al. 1996).
- Increased leg length (Friberg 1982).
- Differences in leg length (Brunet, Cook et al. 1990; Bennell, Matheson et al. 1999; Korpelainen, Orava et al. 2001) or no relationship to injury (Finestone, Shlamkovitch et al. 1991).
- Right leg dominance (Finestone, Shlamkovitch et al. 1991).
- Reduced leg strength (Kowal 1980; Hoffman, Chapnik et al. 1999).
- Large calf circumference has a protective effect (Milgrom 1989; Bennell, Malcolm et al. 1996).
- Ankle inflexibility in dorsiflexion (Messier and Pittala 1988; Fredericson 1996) or increased ankle dorsiflexion (Myburgh, Grobler et al. 1988) or no correlation with injury (Winfield, Moore et al. 1997).
- Narrower tibia (Swissa, Milgrom et al. 1989; Giladi, Milgrom et al. 1991; Beck, Ruff et al. 1996), smaller cross sectional area (Beck, Ruff et al. 1996; Crossley, Bennell et al. 1999), or smaller moment of inertia (Milgrom, Giladi et al. 1989; Beck, Ruff et al. 1996).
- Shorter tibial length (Finestone, Shlamkovitch et al. 1991).

- More external rotation of the hip (Giladi, Milgrom et al. 1987; Finestone, Shlamkovitch et al. 1991; Giladi, Milgrom et al. 1991).
- Narrow pelvis in female Marines (Winfield, Moore et al. 1997).
- Genu valgum (knock knee) (Finestone, Shlamkovitch et al. 1991; Cowan, Jones et al. 1996).
- Hyperpronation (Sommer and Vallentyne 1995).
- Pes cavus (high-arched feet) (Simkin, Leichter et al. 1989; Kaufman, Brodine et al. 1999; Korpelainen, Orava et al. 2001) or pes planus (flat feet) (Sullivan, Warren et al. 1984; Kaufman, Brodine et al. 1999) or no discernible effect of either on injury rate (Montgomery, Nelson et al. 1989; Ilahi and Kohl 1998).
- Forefoot varus (pigeon-toed) (Korpelainen, Orava et al. 2001).

3.5.4 Training Plan Risk Factors

- Changes in training type/intensity (Kowal 1980; Scully and Besterman 1982; Sullivan, Warren et al. 1984; Garcia, Grabhorn et al. 1987; Matheson, Clement et al. 1987; Myburgh, Grobler et al. 1988; Fredericson, Bergman et al. 1995).
- Increase in volume of running per week (Sullivan, Warren et al. 1984; Macera, Pate et al. 1989; Reeder, Dick et al. 1996; Winfield, Moore et al. 1997; Korpelainen, Orava et al. 2001; Hootman, Macera et al. 2002).
- Training in specific subunits (Finestone, Shlamkovitch et al. 1991).
- Cushioning of footwear (Protzman 1979; Greaney, Gerber et al. 1983; Finestone, Shlamkovitch et al. 1992; Fredericson 1996), design of footwear (Reinker and Ozburne 1979) or age of footwear (Gardner, Dziados et al. 1988; Myburgh, Grobler et al. 1988) though no correlation to injury has also been found (Marti, Vader et al. 1988; van Mechelen 1992). The use of cushioned shoes has been shown to produce lower tibial strains (Milgrom, Burr et al. 1996; Milgrom, Burr et al. 1998; Milgrom, Finestone et al. 2001).
- Use of shock-absorbent insoles (Milgrom, Giladi et al. 1985; Simkin, Leichter et al. 1989; Schwellnus, Jordaan et al. 1990) though this has also been found to have no effect on injury rates (Gardner, Dziados et al. 1988).
- Hardness of terrain (Greaney, Gerber et al. 1983; Sullivan, Warren et al. 1984; Shwayhat, Linenger et al. 1994; Fredericson 1996) though other research finds no correlation with injury (Marti, Vader et al. 1988; Brunet, Cook et al. 1990; Shaffer, Brodine et al. 1999).

- Running mechanics (Grimston, Nigg et al. 1994), though other research has found no correlation with injury (Crossley, Bennell et al. 1999).
- Cyclic training (involving interspersed periods of rest) is found to have a protective effect (Churches and Howlett 1982; Scully and Besterman 1982), though others have found no benefit to a rest period (Popovich, Gardner et al. 2000).
- High impact activities (Scully and Besterman 1982; Murguia, Vailas et al. 1988).

3.5.5 Risk Factors Outlook

It is apparent that few of the above listed risk factors are widely reported in the literature without contradiction; exceptions to the rule include previous injury, changes in training, and volume of training. This may be due, in part, to a variation in the quality of investigations in the area of bone overuse injury risk factors; however, this lack of consensus does not appear to be due to a lack of effort or volume of research on the subject matter. In fact, even large studies consisting of hundreds or even thousands of military recruits who undergo numerous measurements—for example, (Greaney, Gerber et al. 1983; Gardner, Dziados et al. 1988; Montgomery, Nelson et al. 1989; Swissa, Milgrom et al. 1989; Milgrom, Finestone et al. 1994; Beck, Ruff et al. 1996; Reynolds, Williams et al. 2000; Lappe, Stegman et al. 2001)—cannot agree on a common set of definitive risk factors for bone overuse injuries in military recruits.

Biomechanical factors, such as those describing anthropometric geometry, may be used to infer how the intrinsic loading of the bones in each individual may vary. In contrast, factors describing demography or personal history may be interpreted to indirectly infer variations in biology which explain how the bones of individuals react differently to a given intrinsic loading. The failure of the available literature to agree on a reliable set of risk factors for predicting bone overuse injuries underscores how imperfect these factors are when used to infer of variations in skeletal geometry and biology.

To illustrate how the biological response to fatigue varies within the skeleton of one individual to the next, it is useful to consider an investigation which studied changes in BMD of 35 military recruits before and after a 12-week boot camp (Pouilles, Bernard et al. 1989). Changes in individual BMD ranged from a net decrease of -6.5% to an overall increase +9%. Clearly, the capability of a subject's individual skeleton to quickly adapt to a new set of fatigue loads strongly influences the chance of a bone overuse injury. Other research (Parfitt 2002) finds that "the coefficient of variation of bone turnover in healthy young women is more than 50% measured histologically, and at least 30% measured biochemically." This is important in that it is these kinds of biological variations which determine those who are prone to bone overuse injuries and those who are less so.

4. Determination of Bone Strain during Locomotion

4.1 Past Work

4.1.1 Biomechanical Models of Human Locomotion

Human locomotion has been a topic of scientific research since the Enlightenment. However, publication in this field—in particular research in biomechanical modeling—has accelerated in the last two decades with the proliferation of high-speed workstations and parallel computing clusters capable of simulating more complex and more realistic systems (Pandy 2001). Still, despite a large volume of recent work on the topic, a definitive understanding of how muscles cooperate to produce human locomotion remains elusive. How the strain fields evolve within bones during walking, running and marching is a topic that has barely been touched.

In fact, most biomechanics models treat bones as rigid links in a pinned system where muscle forces control the rotational moment at each joint and coordinate to reproduce human gait observed in experiment (Hardt 1978; Crowninshield and Brand 1981; Patriarco, Mann et al. 1981; Delp, Loan et al. 1990). Such models have provided a quantitative explanation of how segmental joint powers (inverse dynamics) or muscle dynamics (forward dynamics) cooperate to provide locomotion, but have not yet been extended to provide an understanding of how local strains vary both spatially and temporally within skeletal bones during locomotion.

Inverse Dynamics Models

Inverse dynamics simulations are used to compute joint forces and torques from observed kinematic and ground reaction force data. Inverse dynamics simulations based on an individual's anthropometry and observed gait are useful in determining joint loads from experimentally measured ground reaction forces. This kind of approach is also useful in determining how changes in equipment affect the gait and skeletal loading of an individual (Neptune, Wright et al. 2000). The results of inverse dynamics analyses have been shown to be sensitive to the calculated center of pressure for the measured ground reaction forces (McCaw and DeVita 1995). However, there has been some success at the in vivo experimental determination of functional joint axes (Reinbolt, Schutte et al. 2003) as well as individual body segment parameters such as mass and moment of inertia using anthropometric measurements (Hatze 1980) or kinematic data gathered experimentally (Vaughan, Andrews et al. 1982).

While inverse dynamics models may be formulated in two dimensions (2D, e.g., cycling), simulations of human gait should be three-dimensional (3D) in order to capture torques and rotations in the frontal and horizontal planes (Koopman, Grootenboer et al. 1995; Gilchrist and

Winter 1997; Anderson and Pandy 1999). It has been observed through experiment that 23% of the total work is done in the frontal plane during human locomotion (Eng and Winter 1995). Simulations also show that 2D approaches to this problem may underestimate internal loads by up to 60% (Glitsch and Baumann 1997). Still, some dissent exists, arguing that 2D simulations of walking produce results comparable to 3D simulations (Alkjaer, Simonsen et al. 2001).

Calculation of individual muscle contributions may be important as simulations have shown that coordinated muscular activity can reduce bone bending stresses (Munih and Kralj 1997). Some have argued that the calculation of muscle forces from inverse dynamics calculations is sometimes not reliable (Kautz and Hull 1995; Zajac, Neptune et al. 2002). However, inverse dynamics simulations utilizing optimization methodology have yielded good estimates of muscle force (Hardt 1978; Patriarco, Mann et al. 1981; Brand, Crowninshield et al. 1982; Anderson and Pandy 2003). Muscle forces may be solved for using static optimization (solution of the equations of motion at any given instant in time) or dynamic optimization (solution of the equations of motion over a period of time). It is generally recognized that while dynamic optimization of inverse dynamics models is theoretically closer to the ideal, the use of static optimization is more computationally efficient and produces comparable results (Kuo 1998; Anderson and Pandy 2001). In addition, it has been shown that a weighted least-squares approach to static optimization can be used to correctly predict observed ground reaction forces from kinematic experimental data of simple standing motions (Cahouet, Luc et al. 2002).

Forward Dynamics Models

A separate approach, forward dynamics modeling, predicts kinematic movement of the skeleton from muscle activation inputs (Zajac 1993). The muscle forces are discerned using dynamic optimization methods which set the neural activation of muscles such that the desired motion is produced. Forward dynamics approaches require about a thousand times more computational power than inverse dynamics models (Anderson and Pandy 2001) and are not guaranteed to reproduce all physical aspects of gait. For instance, a forward dynamics model optimized to describe a human running gait was successful at simulating observed ground reaction forces, but did not reproduce observed muscle excitation timing (Neptune, Wright et al. 2000). However, another forward dynamics model optimized to simulate maximum speed cycling by partitioning muscles into alternating functional groups did adequately reproduce experimentally observed muscle excitation signals (Raasch, Zajac et al. 1997). It has been concluded (Anderson and Pandy 2001) that if only muscle and joint forces during gait are required, the use of forward dynamics modeling is not justified since the inverse dynamic approach produces similar results to dynamic models at a fraction of the computational cost.

4.1.2 Finite Element Models of Individual Bones

While inverse dynamics and forward dynamics biomechanical models yield useful data regarding kinematics, joint power, and muscle activity, none currently provide any real insight into the strains seen by the skeleton during locomotion. Some recent research has focused on using finite element modeling (FEM) to understand the local strain state of bone under a constant applied load. Many of these efforts are focused on modeling the skull, mandible, teeth, lumbar vertebrae, femoral head, and associated medical prostheses. However, these approaches tend to be very different from the highly dynamical systems approach of biomechanical models and instead focus on modeling single bones or parts of bones undergoing static loading. Such approaches include three-dimensional FEM simulation of the upper femur (Lu, Taylor et al. 1997; Nilsson 2002; Sakamoto, Tawara et al. 2003), the whole tibia (Ionescu, Conway et al. 2003) and the foot (Camacho, Ledoux et al. 2002). Other research has shown that boundary element modeling (BEM) of the tibia produces similar results to solid-element FEM methods (Muller-Karger, Gonzalez et al. 2001). Some recent FEM simulations of the femur have included more realistic boundary conditions which include statically optimized muscle forces (Duda, Schneider et al. 1997; Duda, Heller et al. 1998; Heller, Duda et al. 1998; Polgar, Gill et al. 2003; Shahar, Banks-Sills et al. 2003). Since the intensity of bone loading (Scully and Besterman 1982; Murguia, Vailas et al. 1988), number of bone loading cycles (Sullivan, Warren et al. 1984; Macera, Pate et al. 1989; Reeder, Dick et al. 1996; Winfield, Moore et al. 1997; Korpelainen, Orava et al. 2001; Hootman, Macera et al. 2002) and reduced bone size (Milgrom, Giladi et al. 1989; Swissa, Milgrom et al. 1989; Giladi, Milgrom et al. 1991; Beck, Ruff et al. 1996; Crossley, Bennell et al. 1999) have all been suggested to be risk factors for bone overuse injuries, models which describe not only joint and muscle force, but also stresses and strains in bone will be critical to analytic approaches which hope to be useful in understanding and predicting bone overuse injuries.

4.1.3 Biomechanical Modeling Outlook

Most biomechanics models describing human motion assume the skeleton is a rigid element and focus on describing the behavior of the muscular system, both in terms of how a single muscle is modeled as well as how groups of muscles coordinate to produce a desired motion (Pandy 2001). As a result, such models do not breach the topic of what strains are generated in bones or the influence of a given repetitive motion on the fatigue life of the skeleton. This is an area which is wide open for new contributions. This is also a research need which must be fulfilled if a predictive model for bone overuse injury is to be formulated.

The time-dependent variation of muscle forces during human gait has not been definitively solved, but it is a current research focus and respected theories and models are

proliferating (Hardt 1978; Crowninshield and Brand 1981; Patriarco, Mann et al. 1981; Happee 1994; Li, Kaufman et al. 1999; Anderson and Pandy 2003). Knowing the muscle and joint forces for a given bone, it is possible to construct a mathematical function for each muscle attachment and joint surface which describes the force it exerts on that bone at any given point in the walking stride. Once the finite element methodology is employed to solve for the local strain fields in the long bones of the legs under static loads, it is a small step to include the mathematical functions describing the muscle force in a FEM simulation of the femur or tibia/fibula, acting at known locations of the associated muscle attachments. This approach provides a close approximation of the local strain field in the long bones of the legs during human locomotion.

4.2 Current Work

We are advancing the state-of-the-art in biomechanics through the development of a three-dimensional musculoskeletal model of the lower extremities of the human body which is used not only for the determination of muscle forces but also the prediction of stresses and strains in bones. This model produces a temporally- and spatially-varying strain field for each long bone of interest which correlates to the loads in the bone due to experimentally observed kinematic gait patterns. This project is therefore a two-pronged approach which utilizes both advanced biomechanical modeling and comprehensive structural analysis. Such an approach is built from a foundation of precise, dependable motion and ground reaction force data collection methods.

The determination of skeletal strains due to the combined effect of ground reaction forces and muscle forces is not new, but it is an area which is underdeveloped. Duda and colleagues (Duda, Schneider et al. 1997; Duda, Heller et al. 1998; Heller, Duda et al. 1998) used a combined biomechanical/FEM model to show that the fully muscled femur is subject to significantly lower bending strains than comparably-loaded femurs with simplified or no muscular loading. This finding has been effectively reproduced in a number of recent works (Polgar, Gill et al. 2003; Shahar, Banks-Sills et al. 2003). Burr and colleagues (Burr, Milgrom et al. 1996) showed that in vivo human tibial strains were found to be 30% lower than they had expected. Other work modeling the tibia (van den Bogert and Nigg 1993) showed that the bending stresses in the tibia during running were affected by running technique and muscle force directions for a simplified muscle model of the lower leg. The musculature of the long bones of the leg has therefore been shown to be not only a torque generator for the joints, but is also a means by which bending stresses are minimized in the long bones during gait, a theory which was first set forth by Pauwels in German in 1950 and republished in English in 1980 (Pauwels 1980).

Other FEM solutions which model only parts of the long bones without the influence of muscle forces will not therefore provide reliable calculations of in vivo skeletal bending strains.

4.2.1 Three-dimensional Musculoskeletal Model of the Lower Extremities

The present musculoskeletal model is based on the renowned model published by Delp and colleagues (Delp, Loan et al. 1990) and later developed into the popular SIMM (Software for Interactive Musculoskeletal Modeling) commercial software package, now distributed by the Motion Analysis Corporation. However, our code was programmed entirely in-house in MATLAB (The MathWorks, Natick, MA). The Delp model is, in turn, largely based on a musculoskeletal model first published by Crowninshield and Brand (Crowninshield 1978; Brand, Crowninshield et al. 1982), with a number of improvements suggested by other authors (Wickiewicz, Roy et al. 1983; Friederich and Brand 1990). The use of a realistic skeletal model is important since variation in the locations of muscular insertions affect the line of muscle action and the overall solution (Duda, Brand et al. 1996). The accuracy of in vivo muscle simulations can be further improved by utilizing MRI imaging data to define details of bony geometries at attachments (Arnold, Salinas et al. 2000). The individual muscles modeled in association with a single leg are listed in Table 1. In addition, we have implemented published values for tibio-patellar motion (Heegaard, Leyvraz et al. 1994; Duda, Heller et al. 1998), mean physiological muscle cross sectional area (Brand, Pedersen et al. 1986), and maximum physiological muscle stress (Crowninshield 1978) into our own version of the model. We have written the source code from the ground up entirely in MATLAB, which enables maximum flexibility in model development while accelerating design time by utilizing a number of the commercially-available MATLAB toolboxes, including the Optimization Toolbox and the Signal Processing Toolbox.

4.2.2 Inverse Dynamics Analysis

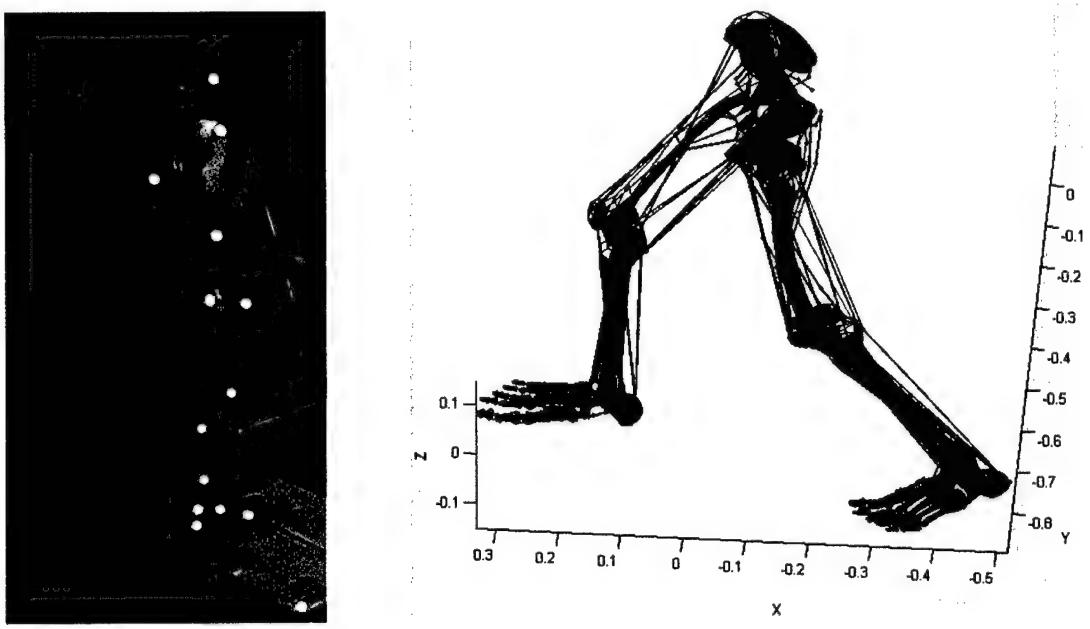
By tracking kinematic motion experimentally from markers on walking subjects, it is possible to infer joint angles as a function of time and implement the observed motion in the musculoskeletal simulation, as illustrated in Figure 1. Using published relations for individual muscle forces versus time, it is then also possible to reconstruct effective motor moments at the joints as depicted in Figure 2. Our code has been validated by reproducing joint torque data published by three separate authors using the muscle force data they present in their papers (Crowninshield 1978; Hardt 1978; Patriarco, Mann et al. 1981).

Table 1: Muscles Explicitly Modeled in the Three-dimensional Musculoskeletal Model.

Gluteus medius (anterior compartment)	Iliacus
Gluteus medius (middle compartment)	Psoas
Gluteus medius (posterior compartment)	Quadatus femoris
Gluteus minimus (anterior compartment)	Gemelli
Gluteus minimus (middle compartment)	Periformis
Gluteus minimus (posterior compartment)	Rectus femoris
Semimembranosus	Vastus medialis
Semitendinosus	Vastus intermedius
Biceps femoris (long head)	Vastus lateralis
Biceps femoris (short head)	Gastrocnemius (medial head)
Sartorius	Gastrocnemius (lateral head)
Adductor longus	Soleus
Adductor brevis	Tibialis posterior
Adductor magnus (superior component)	Flexor digitorus longus
Adductor magnus (middle component)	Flexor hallucis longus
Adductor magnus (inferior component)	Tibialis anterior
Tensor faciae latae	Peroneus brevis
Pectineus	Peroneus longus
Gracilis	Peroneus tertius
Gluteus maximus (superior compartment)	Extensor digitorus longus
Gluteus maximus (middle compartment)	Extensor hallucis longus
Gluteus maximus (inferior compartment)	

The determination of net joint moments from individual muscle forces—as well as the determination of bone strains—requires precise knowledge of the magnitude, direction and location of the muscle forces on the bone surface. This information is provided for each time step in the gait cycle using our musculoskeletal model, as shown in Figure 3. Each muscle is modeled as a line which acts through the physiological centroid of the actual muscle (Brand, Crowninshield et al. 1982). This data can also be employed in conjunction with joint reaction force data obtained using inverse dynamics analysis to determine the physiological loading conditions for each bone at any point in the gait cycle.

A number of "wrapping points" are added to some muscles to ensure that the simulated line of action of the muscle resembles the true path of the actual muscle belly (Delp, Loan et al. 1990). Some of these wrapping points become active only for certain joint angles. For instance, the vasti or "quads", which stretch from the hip joint to the patella, are modeled with extra wrapping points over the distal head of the femur which become active for angles of knee dorsi-flexion greater than 70 degrees. The inclusion of these wrapping points is critical to enhancing the model's predictive ability since the wrapping points ensure that the proper effective muscle force line of action is described when performing joint torque calculations based on muscle activity.



(a) (b)

Figure 1: (a) Picture illustrating the use of visual markers and a force plate to gather kinematic and ground reaction force data from the subject at USARIEM and (b) a rendering of the three-dimensional musculoskeletal model of the lower extremities, based on that developed by Delp and colleagues (1990).

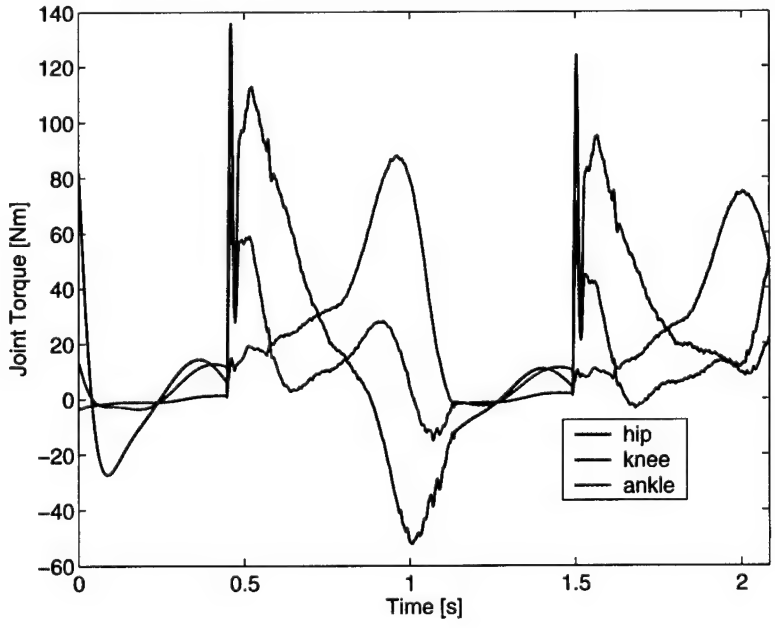


Figure 2: Joint torque data determined directly from the 3D musculoskeletal model and experimental kinematic and ground reaction force data gathered by USARIEM.

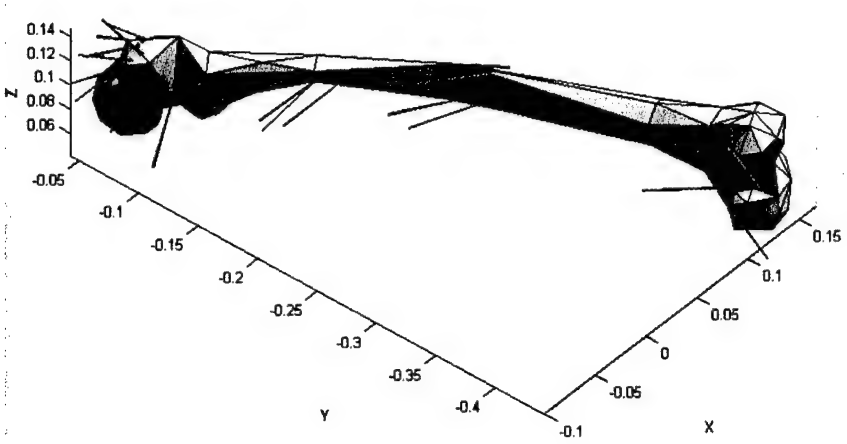


Figure 3: Muscle force directions for the femur while in a given stance during normal gait, determined through three-dimensional biomechanical analysis.

4.2.3 Static Optimization of Muscle Forces

While it is important to be able to properly calculate joint moments from individual muscle forces, it is even more significant to solve the redundant problem of determining individual muscle activation patterns which match joint torques determined through inverse dynamics analysis of experimental motion data. We have achieved this end by applying constrained static optimization methods (Hardt 1978; Pedotti, Krishnan et al. 1978; Crowninshield and Brand 1981; Li, Kaufman et al. 1999). The results of such an optimization are shown in Figure 4.

Static optimization is achieved through the iterative minimization of a particular objective function, subject to certain constraints. The constraints for our problem are clear: Each muscle may only generate force along its physiologic centroid and within the range of its maximum force or maximum physiological stress. Muscles only generate tensile forces on their tendonous insertions. The net sum of all muscle torques about a joint is equal to the joint moment required for locomotion. What is not as clear is the form of the objective function to be minimized. Some researchers have suggested the use of total muscle force as a linear objective function (Seireg and Arvikar 1973; Patriarco, Mann et al. 1981; Li, Kaufman et al. 1999); however, such an approach can lead to small muscle groups acting at a disproportionately high percentage of their maximum tensile force as compared to larger neighboring muscle groups. This is not a physically realistic scenario. Alternatively, other research has suggested incorporating the physiological cross sectional area of each muscle—which directly relates to force generating ability—by minimizing a stress-based or weighted force objective function (Brand, Pedersen et al. 1986; Li, Kaufman et al. 1999) and this has been found to generate more realistic muscle force

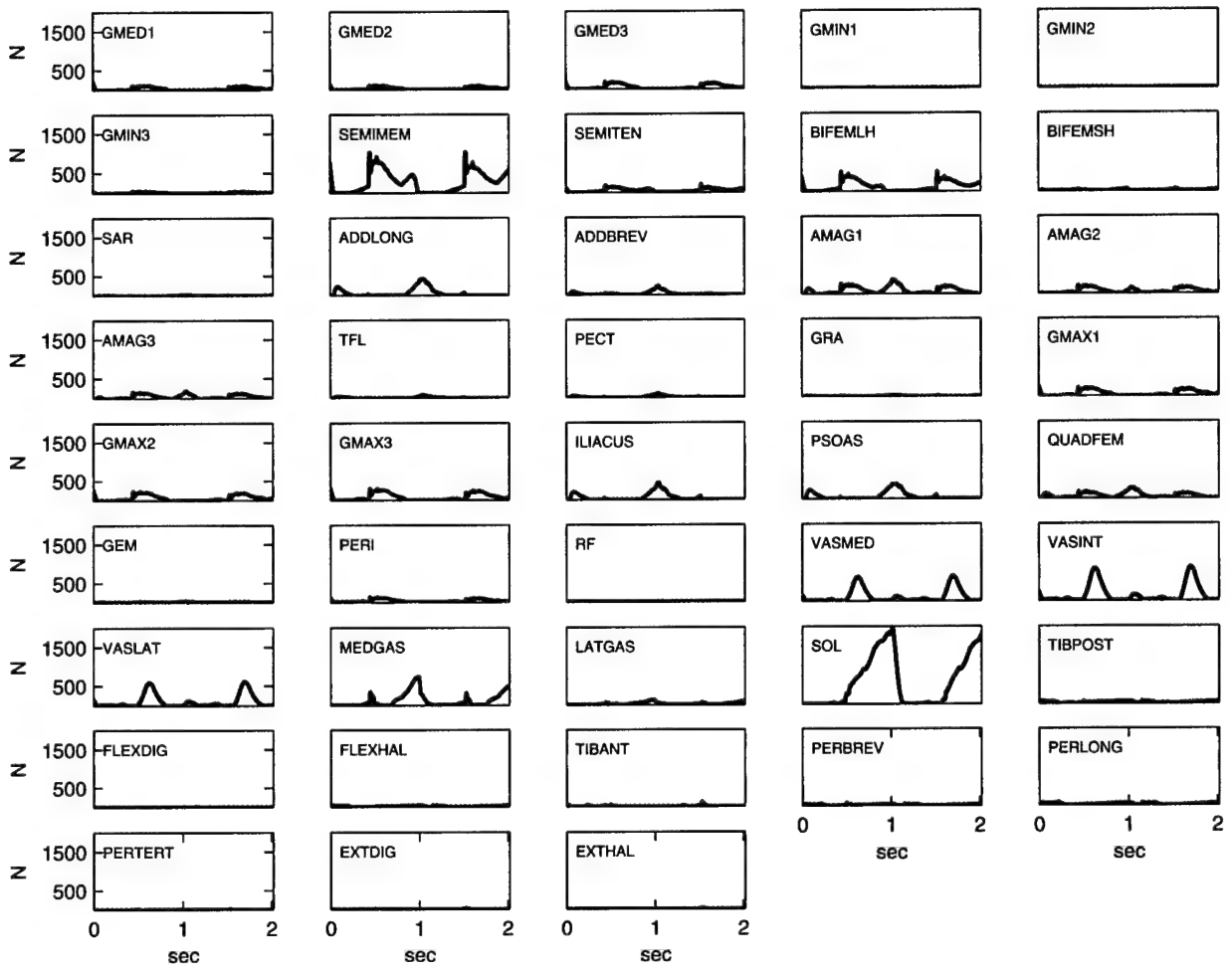


Figure 4: Muscle force plots of 43 muscles in a leg, predicted using static optimization based on the experimental kinematic and ground reaction force data supplied by USARIEM.

activation patterns. The minimization of muscle energy (Hardt 1978) and a muscle fatigue criterion (Dul, Townsend et al. 1984) have also been suggested as optimization objectives. These approaches have the benefit that biochemical kinetics can be incorporated in the muscle force calculations, making them more physically meaningful, though such criteria require parameters which are often not available. When nonlinear objective functions are used (e.g., force or stress taken to the second or third power), it has been found that synergistic muscle behavior, similar to that observed in experiment, is predicted (Dul, Townsend et al. 1984).

It is also difficult to determine which of these ad hoc objective functions is most correct since reliable experimental observations of muscle activation patterns during gait remain unavailable. Electromyography, or EMG, is a popular method for inferring surface muscle activation from electrophysiological signals picked up using skin mounted electrodes. However, the magnitude of the signal received is subject to a number of difficult to control

variables such as signal interference (hum), signal acquisition problems (clipping, baseline drift, or skin artifacts), and signal processing errors. As such, EMG is only useful for determining when muscles may be active and is unreliable in determining muscle force magnitude. In addition, EMG is unable to determine when deep muscles, which do not pass directly under the surface of the skin, are active.

However, the choice of optimization criterion may not be as important as once thought. A comparison between different objective functions used in static optimization revealed that a muscle fatigue-based criterion produced similar results to a metabolic energy-based criterion, suggesting that a time-independent performance criterion is not a significant model limitation (Anderson and Pandy 2001). Some research has found that the muscle force solution is not particularly sensitive to the particular ad hoc optimization criterion applied (Li, Kaufman et al. 1999) while other research has been able to discriminate nonlinear objective functions as promoting load sharing among muscles more than linear objectives (Dul, Townsend et al. 1984). In short, there is evidence that the static optimization of muscle force is not particularly sensitive to the exact form of the objective function minimized, as long as a nonlinear objective function is employed. This finding may be due to the small domain of muscle force solution sets which fulfill the joint torque constraints.

In fact, one reason that it is important to use a 3D musculoskeletal model instead of a 2D model is that nearly all of the muscles in the lower extremity create joint torques in different planes compared to the desired direction of joint torque. As a result, the 3D models properly capture antagonistic muscle action—which counterbalances out-of-plane muscle forces for a movement in a desired plane—which is not found in simplified planar models. (Pedersen, Brand et al. 1987). This need to counterbalance potentially injurious out-of-plane forces in the solution could reduce the solution domain significantly.

Some researchers have called for the eventual abandonment of ad hoc objective functions associated with inverse dynamics optimization methods in lieu of more physically-based muscle activation criteria (Epstein and Herzog 2003). Such criteria are most readily applied in the forward dynamics framework. Alternative forward dynamics models are computationally expensive and have not been shown to have a predictive advantage in applications where inverse dynamics can also be applied (Anderson and Pandy 2001). Therefore, the static optimization of muscle force based on joint torques obtained from inverse dynamics analysis still appears to be the best method at the present time for studying human gait.

4.2.4 *Finite Element Modeling of the Long Bones*

A finite element model of femur is being developed to study strain field variations during human locomotion. The geometry of the femoral model was reconstructed from the male computed tomographic (CT) dataset of the Visible Human Project, which is maintained by the National Library of Medicine. First, contours were mapped onto each sectional CT image. These contours distinguish bone from the surrounding soft tissues. The contours were then connected to form polygons which represent the periosteal and endosteal bone surfaces. Finally, a volume representation of the femur was created from the polygonal surfaces and the original DICOM files. The DICOM (Digital Imaging and Communications in Medicine) image file standard is maintained by the National Electrical Manufacturer's Association (NEMA) in Rosslyn, Virginia. The simulated femoral volume is shown in Figure 5(a).

The three-dimensional FEM grid was created using TrueGrid® (XYZ Scientific Applications, Inc.). A mesh of hexahedral elements was projected between the simulated endosteal and periosteal femoral surfaces. We were able to achieve different levels of grid refinement using a simple set of parameters embedded in the TrueGrid® mesh template. The bone material properties used in the FEM simulation were obtained directly from information in the DICOM images. Each pixel of a DICOM image has a *CT number* associated with it. The CT number, also referred to as a *Hounsfield unit*, represents the X-ray absorption rate of a given pixel in the bone's cross section. In this way, the CT number gives an estimate of the density of a pixel. The effective density of the pixel is determined using the linear relationship

$$\rho_{eff} = A \times CT + 1000\left[\mathrm{kg/m^3}\right],$$

where ρ_{eff} is the effective density, CT is the CT number, and A is a machine-dependent correction factor which has been reported as 0.523 (Rho, Hobatho et al. 1995) and 0.464 (Taylor, Roland et al. 2002). We set A to the value of 0.523 since this is the most commonly used value used for similar bone models in the literature. The elastic modulus was then estimated from the effective density using the equation (Goldstein, Matthews et al. 1991)

$$E\left[\mathrm{MPa}\right] = \begin{cases} 1352\rho_{eff}^{1.48} & 0 < \rho_{eff} < 1.4\left[\mathrm{g/cm^3}\right] \\ 34623\rho_{eff} - 46246 & 1.4 \le \rho_{eff} < 2.0\left[\mathrm{g/cm^3}\right] \end{cases}.$$

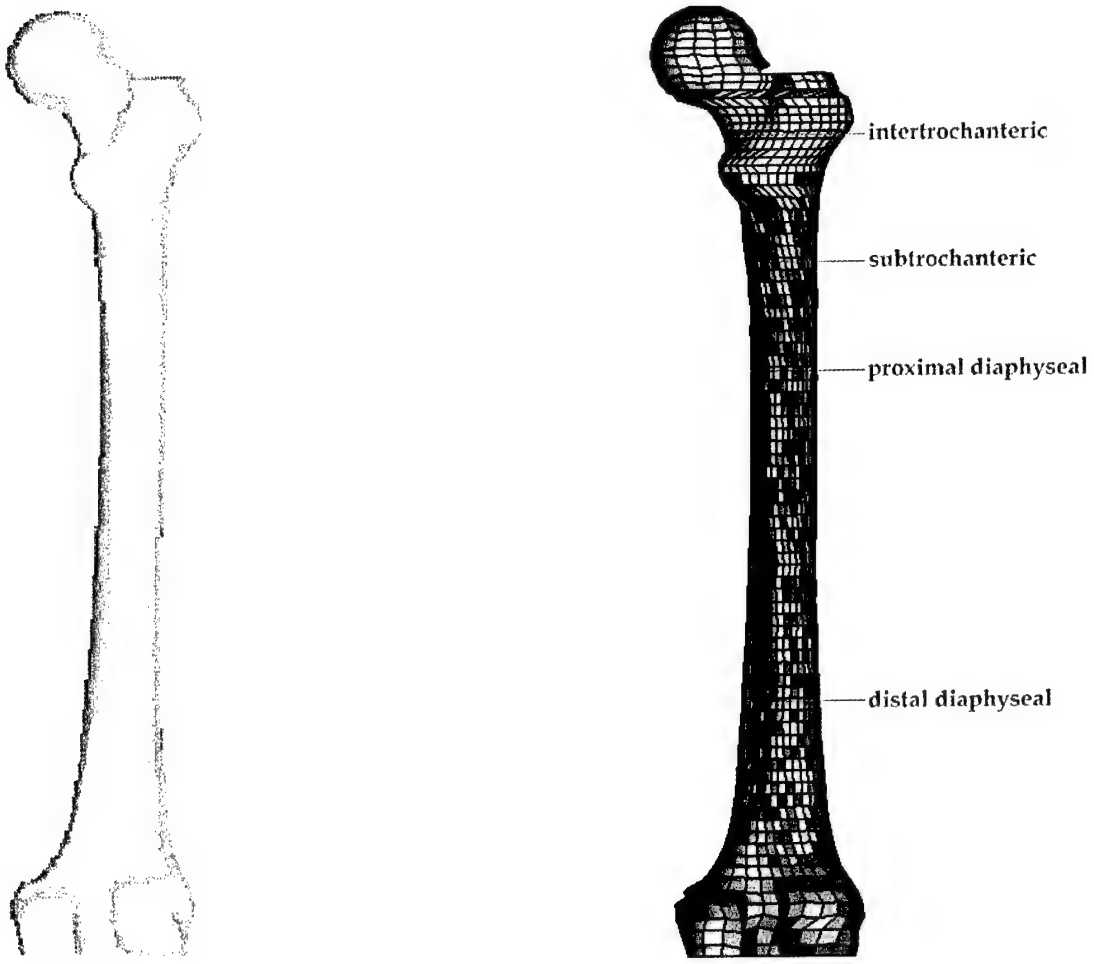


Figure 5: (a) Femur volume representation based on CT scan data obtained from the Visible Human Project and (b) finite element model developed in-house in TrueGrid based on the Visible Human data. Neighboring elements with differing material properties are shaded with differing colors. Section layout similar to that of (Polgar, Gill et al. 2003).

The elastic modulus and mass density of each element is based on the average local CT image data within that element, with the exception of the proximal and distal fifths of the femur which were assigned a uniform modulus of 20 GPa. The other elements were assigned an elastic modulus in the range of 5-35 GPa.

A method similar to ours had been used previously in the construction of the Muscle Standardized Femur (MSF) model (Viceconti, Ansaloni et al. 2002; Polgar, Gill et al. 2003), which has become the de facto standard in the biomechanical modeling community. The model is freely available for research use from the International Society of Biomechanics (ISB) mesh repository. We chose to develop our own model instead of using this one because the FEM code we used, LS-Dyna, requires the use of particular elements (8-node blocks, 6-node wedges and 4-node elements) which are not the same as those used in the MSF model.

FEM model of the femur with joint torques and forces

The FEM simulation was performed in LS-Dyna (Livermore Software Technology Corporation, Livermore, CA), a solver that specializes in finite strain, high strain rate applications. This software was chosen because of our current proficiency in this package and the possibility that the biomechanical model used could later be extended to the simulation of impact loading scenarios. A fixed boundary condition was applied to the proximal head of the simulated femur. A constrained femoral head has been found to provide a more accurate representation of bone loading in the absence of the explicit representation of all muscle forces (Simoes, Vaz et al. 2000). Three-dimensional vector loads representing joint force and joint torque were applied at the femoral condyles. The boundary conditions employed in the current model are highly simplified approximations of the actual forces and constraints the femur is exposed to in vivo. We will incorporate increasing degrees of realism into the model as we develop it further.

Simulations were run to determine the bone strains resulting from simplified joint loadings (e.g., joint force and joint torque) determined through inverse dynamic analysis of experimental video and force plate data. The FEM simulations utilizing simplified joint loads shows that femoral strains vary within the bone and with different gait patterns. The results of two of these simulations are summarized by Figure 6, which plots the maximum principal strain within the four femoral cross sections illustrated in Figure 5(b). Each curve represents the maximum tensile strain (i.e., the first principal strain) with each cross section at a given time.

These plots illustrate the degree of variability in the tensile strain which can exist within different locations in the bone as well as between different subjects. For instance, while the gait pattern of subject S1P6T2 produces a greater principal strain within the proximal diaphyseal section as compared to subject S2P6T1, the converse is true within the distal diaphysis. The recognition of such a pattern between two patients could help in the diagnosis of why one patient is more susceptible to overuse injury at a particular level in the femur relative to the other patient. However, in order to obtain a more realistic loading scenario the torque motors inferred to exist at the joints by inverse dynamics analysis must be replaced by physiologically consistent muscle forces acting at anatomically correct locations on the bone surface.

FEM Model of the Femur with Joint and Muscle Forces

We incorporated muscle forces into the FEM model by performing a static optimization for muscle force using the joint torques determined through the inverse dynamics analysis as a constraint, as described in a previous section. The optimization was set-up using the three-dimensional musculoskeletal model, also described previously. The muscle forces are currently modeled as three-dimensional vector point loads with variable amplitudes and directions. Later in the project we plan to enhance the realism of the musculoskeletal model by replacing the muscular point forces with stresses or pressures over their anatomic areas of muscle insertion. At the knee, the joint forces obtained via inverse dynamics analysis were applied to the femoral condyles to approximate the joint contact loads. In reality, these joint forces form a lower boundary for the true joint contact forces. The muscle forces acting across joints supplement the weight-bearing forces predicted using inverse dynamics; this joint contact load increases with greater amounts of antagonistic muscle action (Winter 1990). The four femoral cross sections depicted in Figure 5(b) were again investigated to illustrate the variation of the maximum principal strains within the femur during one step of walking. The FEM analysis result of the gait pattern of subject S1P6T2, shown previously in Figure 6, is now compared with the incorporation of muscle forces in the model in Figure 7.

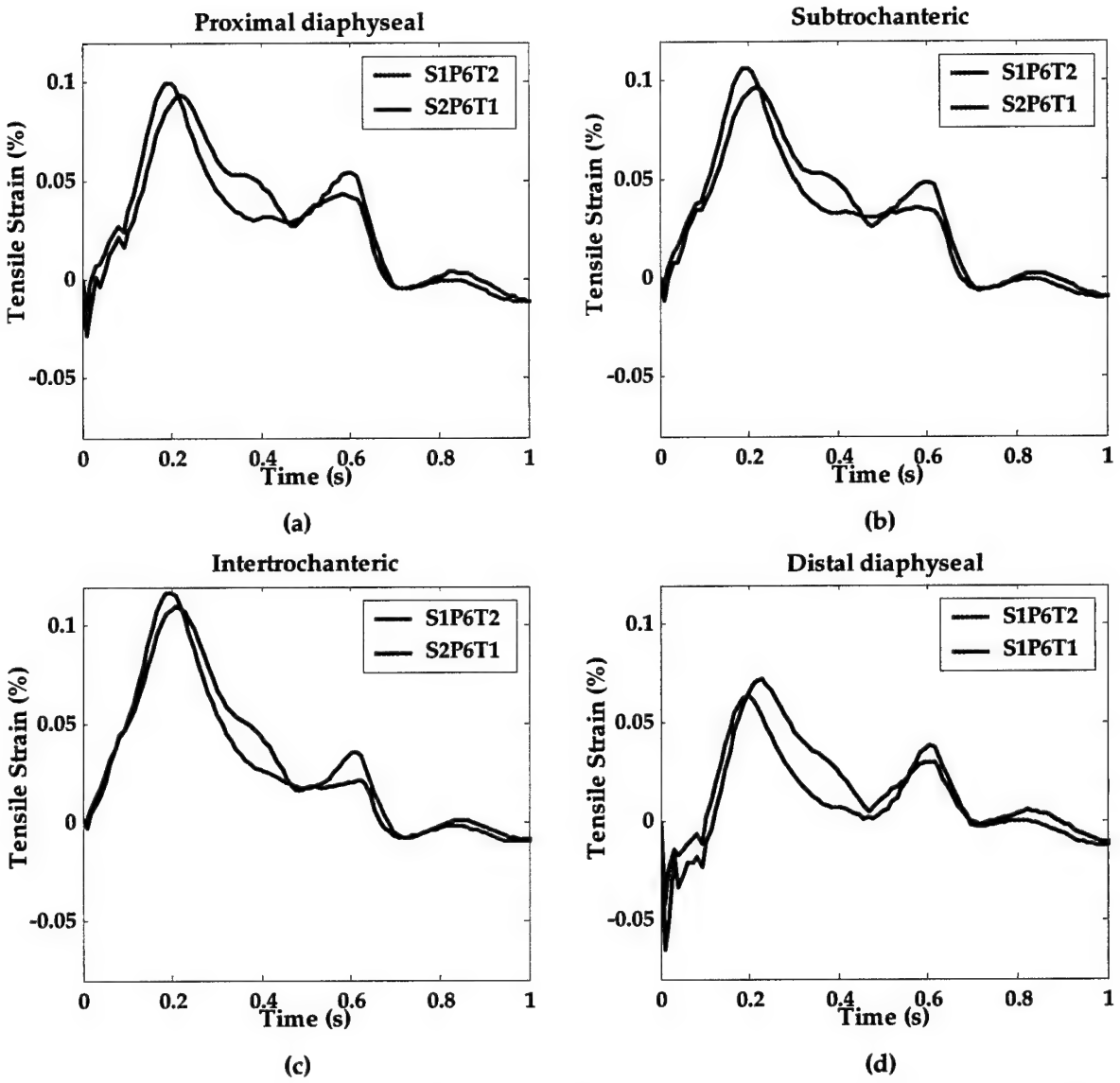


Figure 6: Maximum tensile strains arising in the simulated femur due to joint torque and joint force boundary conditions determined from inverse dynamics analysis of three experimental trials at the (a) intertrochanteric section, (b) subtrochanteric section, (c) proximal diaphyseal section, and (d) distal diaphyseal section. See Figure 5(b) for a further description of these sections.

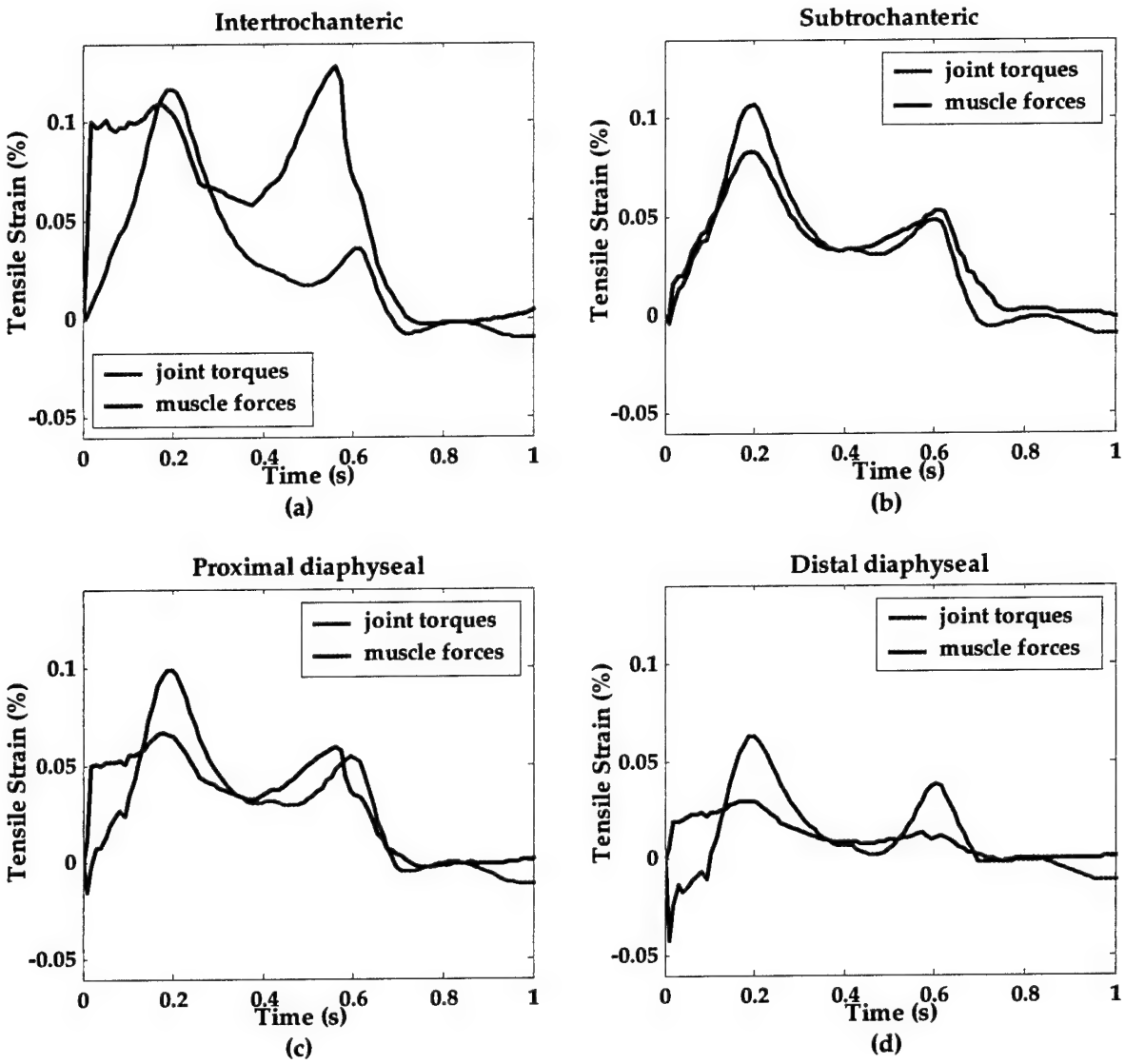
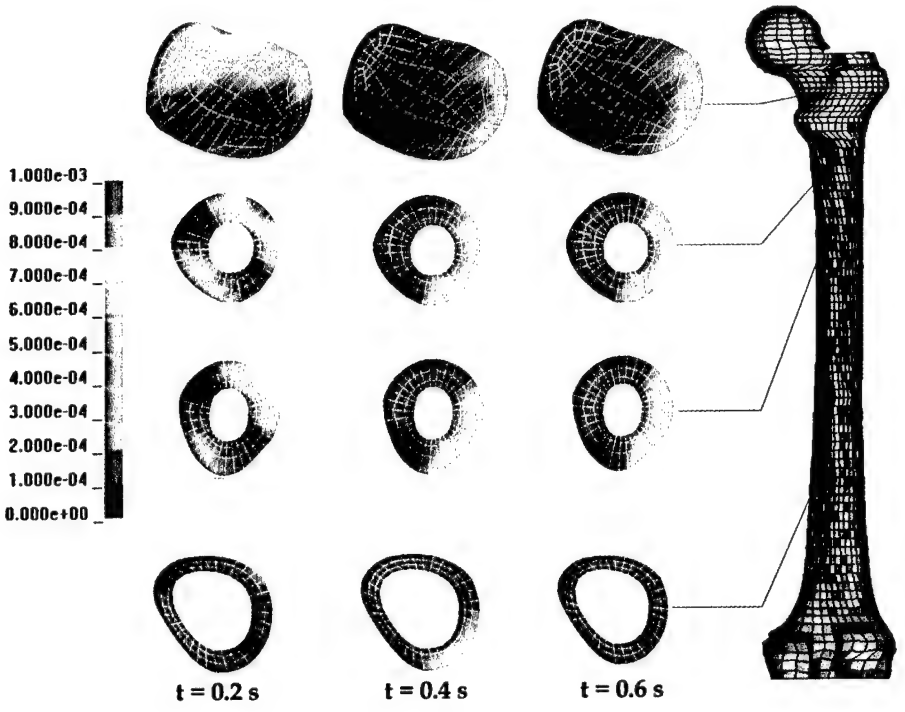


Figure 7: Maximum tensile strains arising in the simulated femur due to joint torque and joint force boundary conditions determined in subject S1P6T2 from inverse dynamics analysis of three experimental trials at the (a) intertrochanteric section, (b) subtrochanteric section, (c) proximal diaphyseal section, and (d) distal diaphyseal section. See Figure 5(b) for a further description of these sections.

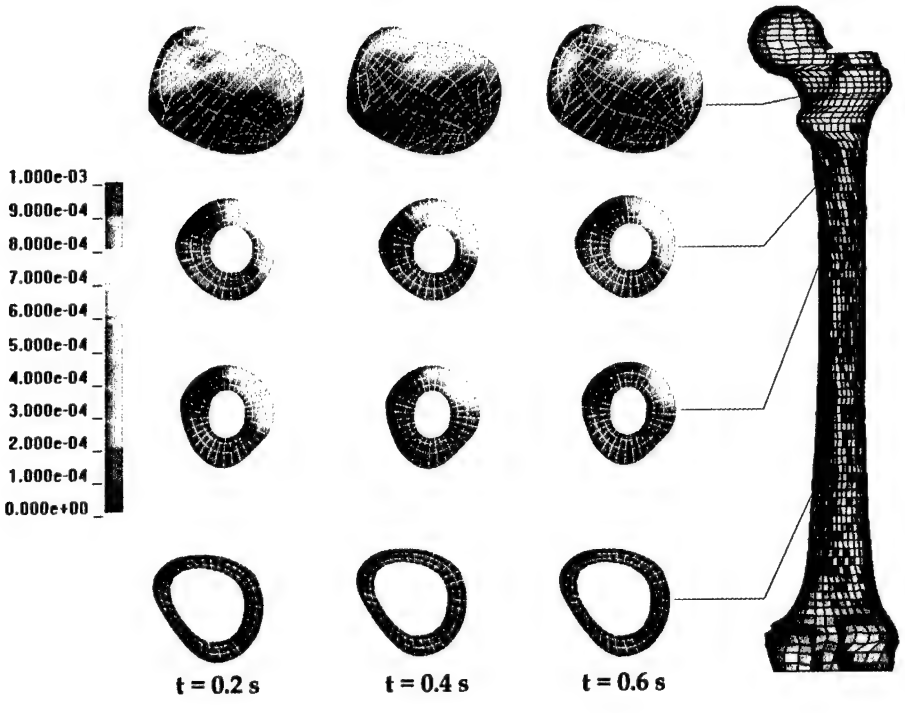
It is observed from Figure 7 that the inclusion of muscular forces tends to, in general, reduce the maximum tensile strains in the simulated femur. This is most evident within the distal diaphysis, plotted in Figure 7(d). The exception to this finding appears within the intertrochanteric section (i.e., between the greater trochanter and lesser trochanter) in Figure 7(a) where greater tensile strains arose within the muscle force model as compared to the joint torque model between 0.3 s and 0.8 s. However, this section is very close to the constrained femoral head, which is a simplified boundary condition compared to the in vivo condition. Therefore, the results from this simulation should be considered preliminary and are primarily useful for illustrating the differences between the strains predicted by a comprehensive musculoskeletal model and those predicted by a simplified skeletal model.

Even in the adolescent state of our model, the effect of explicitly modeling muscle forces is evident in the bone strain fields shown in Figure 8, Figure 9, Figure 10, and Figure 11. Muscle forces have the effect of averaging the tensile strain fields, as shown by Figure 8 and Figure 9. Even with the simplified boundary conditions applied, it can be seen that the model which does not account for muscle forces (Figure 8(a) and Figure 9(a)), produces large amounts of bone strain over greater bone volumes than the model which does account for muscular action (Figure 8(b) and Figure 9(b)). This logically implies that the body may be constructed such that muscle forces fulfill the dual purpose of torque generation as well as reduction of tensile bone strains. The effect of the inclusion of muscle forces on compressive strains—shown in Figure 10 and Figure 11—is less marked, but is still significant. Most notably, muscle forces reduce compressive strain concentrations in the more distal parts of the bone. The finding that the muscle forces virtually eliminate the strain gradient observed in the distal diaphysis shown in Figure 10(a), is consistent with the notion that muscles act to minimize bending strains in the femur (Duda, Heller et al. 1998). It is also noteworthy that the effect of muscle forces on femoral compressive strain becomes more marked further from the simplified boundary constraint imposed on the femoral head. Further enhancements of the realism of the model will likely reinforce the notion of the stabilizing and protective effect skeletal muscles have.

Our results and findings correlate well with previous research published by Duda and colleagues (Duda, Brand et al. 1996; Duda, Schneider et al. 1997; Duda, Heller et al. 1998; Heller, Duda et al. 1998) who have performed similar studies. They found that periosteal surface strains peaked below 0.2 in their musculoskeletal model. This result corroborates with our results which find bone strains mostly below 0.15 in our simulations. We have further found that the largest strains in our musculoskeletal model were compressive in nature.

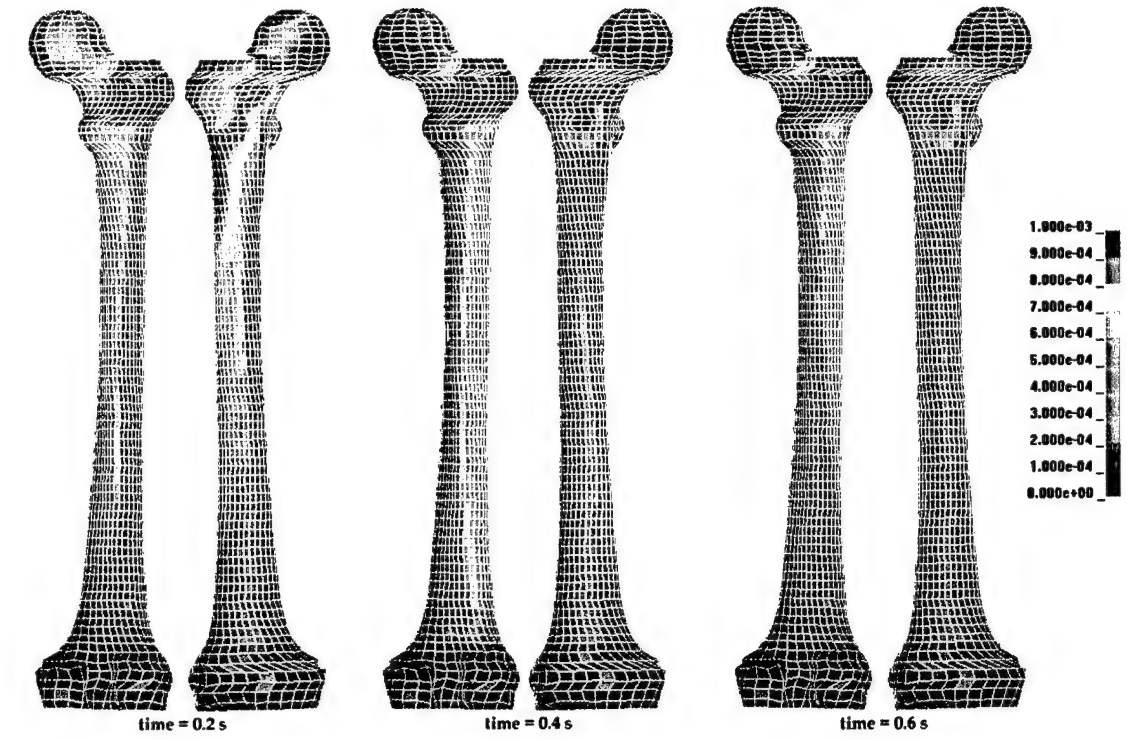


(a)

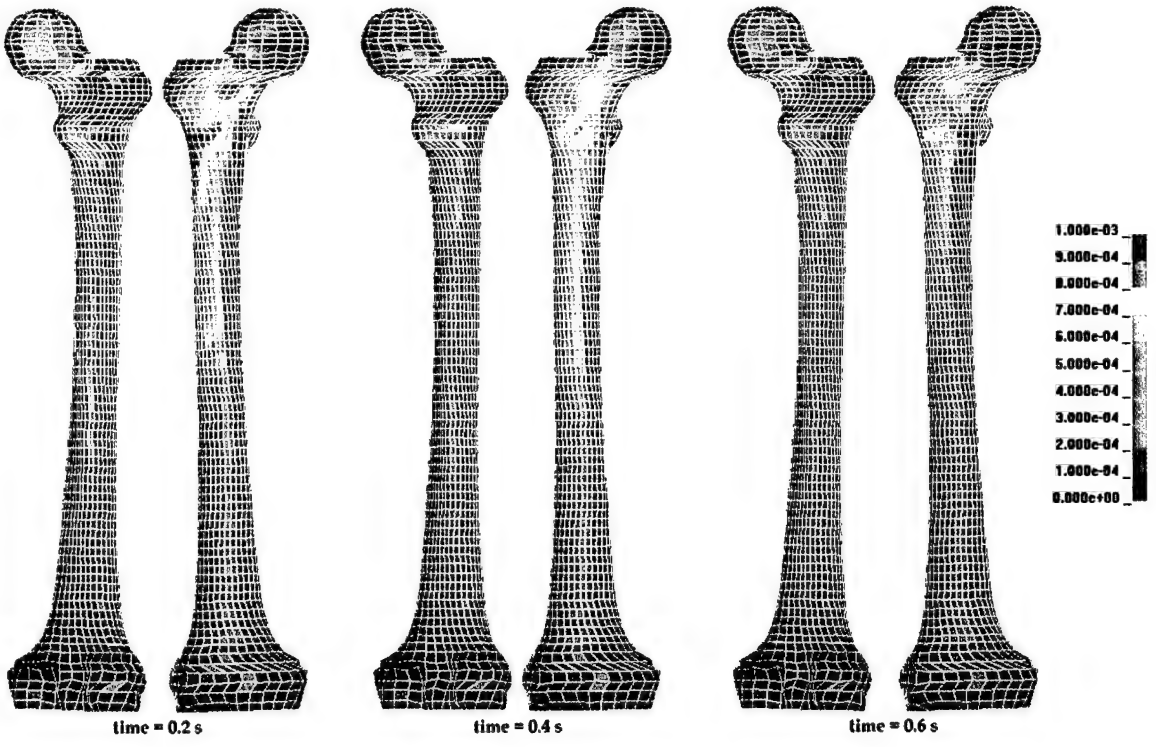


(b)

Figure 8: FEM simulation results showing tensile strain (i.e., 1st principal strain) of bone cross sections during normal gait for subject S1P6T2 when (a) joint torque and force boundary conditions and (b) muscle force and joint force boundary conditions are imposed.

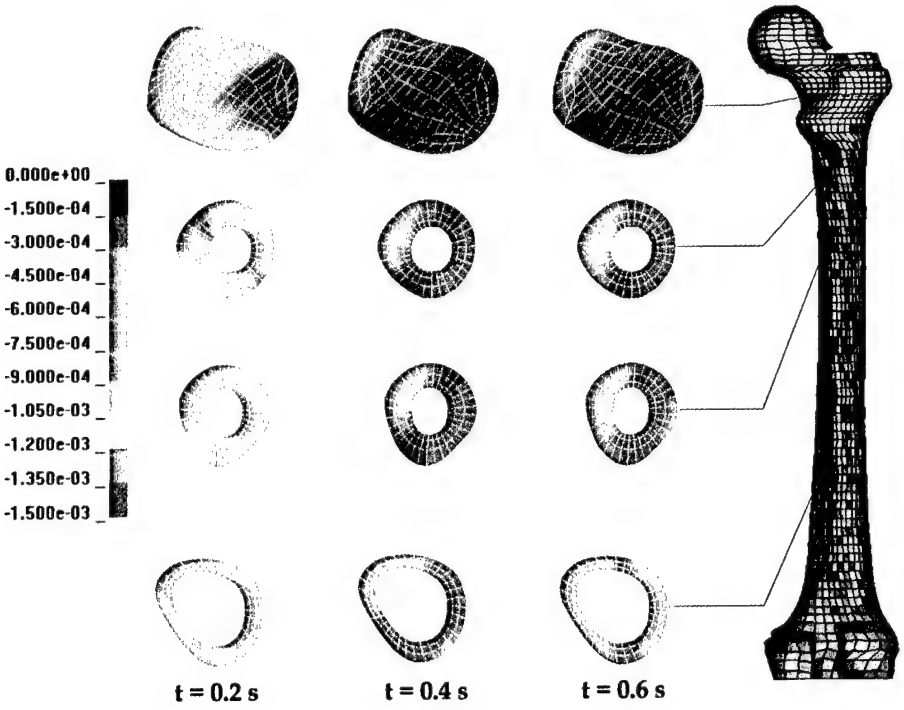


(a)

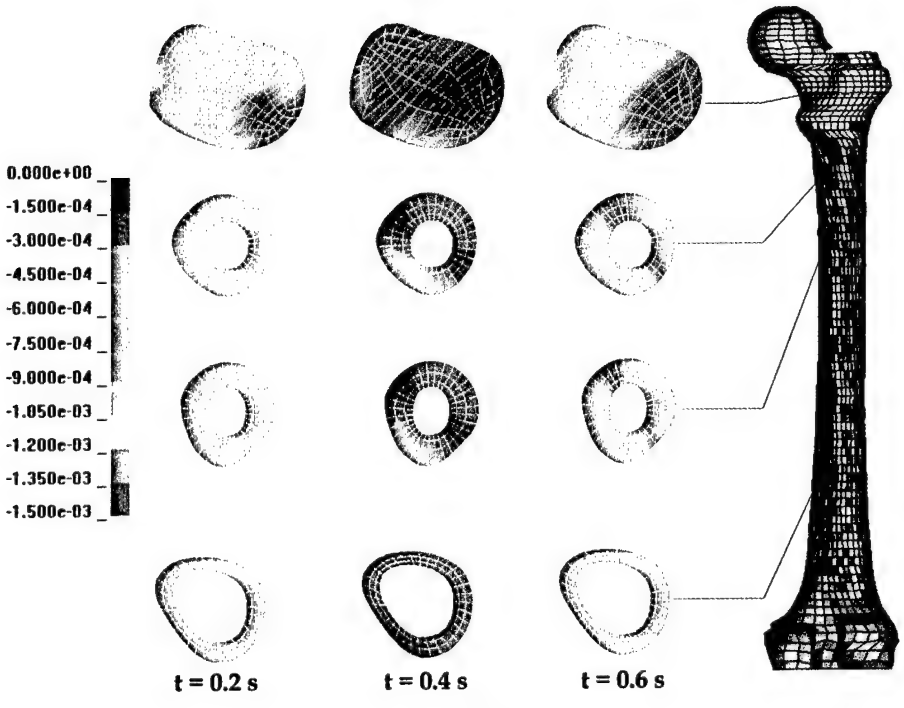


(b)

Figure 9: FEM simulation results showing periosteal tensile strain (i.e., 1st principal strain) during normal gait for subject S1P6T2 when (a) joint torque and force boundary conditions and (b) muscle force and joint force boundary conditions are imposed.

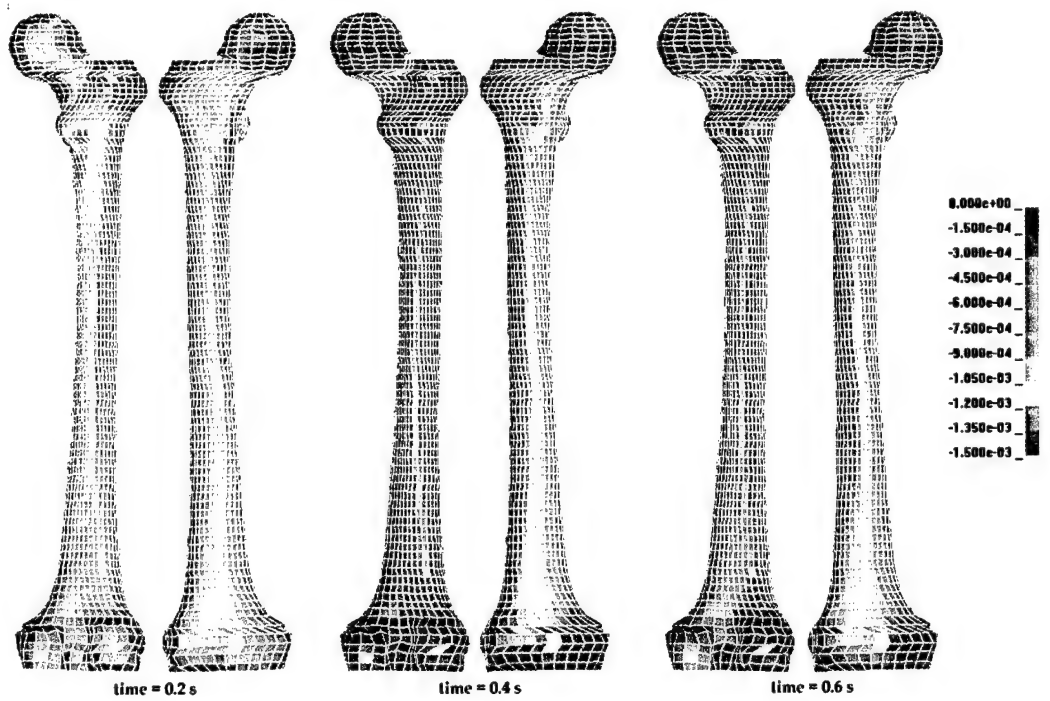


(a)

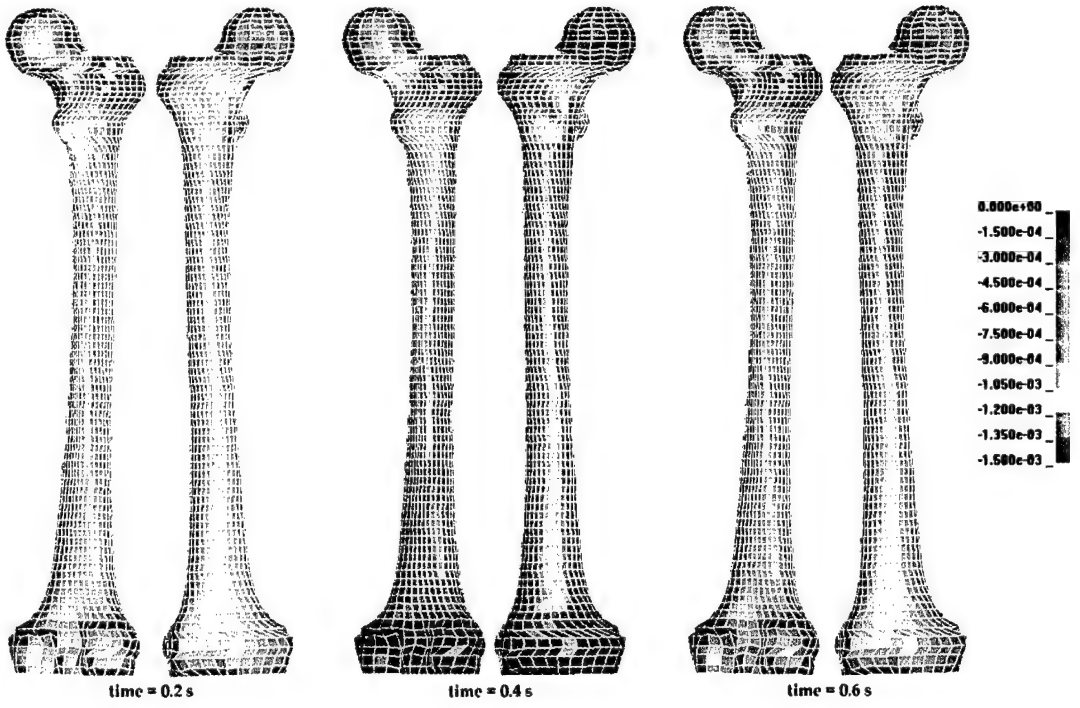


(b)

Figure 10: FEM simulation results showing compressive strain (i.e., 3rd principal strain) of bone cross sections during normal gait for subject S1P6T2 when (a) joint torque and force boundary conditions and (b) muscle force and joint force boundary conditions are imposed.



(a)



(b)

Figure 11: FEM simulation results showing periosteal compressive strain (i.e., 3rd principal strain) during normal gait for subject S1P6T2 when (a) joint torque and force boundary conditions and (b) muscle force and joint force boundary conditions are imposed.

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5. Quantification of Descriptive Training Data

5.1 Current State-of-the-Art

The development of an overuse injury model, as discussed in the previous chapter, highlighted the importance of strain magnitude and frequency as two factors which significantly influence the probability of bone overuse injury. The direct measurement of these bone loading parameters is an admirable goal, but is unfortunately infeasible with current technology. This is particularly true for the many important studies which examine large groups of subjects outside of the laboratory and over extended periods of time. The strains which load bearing bones see during basic training are basically unknown. Thus, a key component of our effort to better predict bone overuse injuries is an accurate representation of the loads experienced during training.

The training data currently available is composed primarily of general descriptions of daily training activities (i.e., training plan outlines). Such descriptions may include the time to completion for an obstacle course or the distance covered during a long run or march. However, these datasets are descriptive of the activity performed—not the specific loading on the human skeleton—and are therefore ill-suited for use as direct input for a biomechanical model. Thus, a method of quantifying general training descriptions in terms of scientific parameters such as strain range and loading frequency is necessary for further progress in the development of an overuse injury model.

5.2 New Contributions

A literature review has been conducted with the purpose of developing regression equations relating speed to ground reaction forces and loading frequency, both of which affect the rate of bone fatigue. Early stages of this literature review were presented in the 2002 Annual Report (Sih, Shen et al. 2003). Variables studied included step length, step rate, and foot contact time as well as peak braking, propulsive and vertical forces. In conjunction with this review, we derived a set of regression equations to aid in the quantification of training regimens. Additional studies have now been analyzed and the regression relations have been further improved with statistical guidance from the Naval Health Research Center. The equations are shown in Table 2 and Table 3. The data used in the regression analysis was acquired from approximately 763 subjects under speeds ranging from 0.25 to 3.0 m/s for walking and 571 subjects running at speeds from 1.0 to 10.9 m/s.

The regression relations we have found predict the GRF and loading frequencies during human gait for situations when such data is not readily accessible, such as studies involving

large populations. In addition, these relations can be used to determine the degree variability of these gait measures across such populations. They also provide researchers with a method for making an objective comparison between data collected from different biomechanical sensors and protocols. The regression equations and data were plotted to allow researchers to easily compare our findings to their own results. To maximize the utility of this analysis, we have sought the largest sample size possible within which a variety of diverse data collection methods were used. We find that regressions for step length and step rate for both walking and running fit the observed data quite well but there is less of a consensus within the published data for GRFs at higher speeds of walking and running. We find that regressions for step length and step rate for both walking and running fit the observed data quite well but there is less consensus within the published data for GRF's at higher speeds of walking and running. We have submitted our findings in a manuscript entitled, "Timing and ground reaction force estimates for normal human walking and running at a variety of speeds: a survey of the literature," which is currently being considered by the Journal of Biomechanics as an original article. The draft submitted is in the appendix of this report.

While these regression equations serve as the initial method to quantify training regimen data, they have several limitations that currently mitigate their predictive potential. First, our current analysis only quantifies two of the most common movements experienced during training: walking and running. Other movements, such as jumping and climbing, may contribute to bone strain and fatigue, yet are not typically described with sufficient detail in the training records. For example, additional exercises such as circuit and obstacle courses are not included in training mileage but may significantly influence bone fatigue. Also, while distance measures are general descriptors of walking and running, without additional information such as velocity and terrain, bone strain magnitude and frequency cannot be completely described. Second, the regression equations developed are representative of the average value expected for a general population and does not yet account for individual variability in size, fitness, or gait style. Third, since the training plan outlines are drawn up prescriptively rather than descriptively, undocumented changes made by drill instructors are not necessarily recorded. Thus, there is a need for a more complete approach to the quantification of the training performed. As mentioned earlier, studies that have looked at distances marched and run as possible correlates to bone loading history have met with limited success (e.g., (Popovich, Gardner et al. 2000)).

Table 2: Best fit regression equations for walking gait parameters based on gait velocity, V ($m \cdot s^{-1}$). Velocity range and approximate number of subjects (N) are included.

	Regression Equation	R^2	V Range	N
Gait Timing				
SL (m)	$0.6230 \cdot V^{0.4812}$	0.86	0.25 - 3.0	655
SR (steps/sec)	$1.6062 \cdot V^{0.5175}$	0.88	0.25 - 3.0	655
t_c (sec)	$-0.3794 \cdot \mathrm{Ln}(V) + 0.7607$	0.60	0.5 - 3.0	318
Ground reaction forces (BW)				
GRF_{Brake}	$-0.0259 \cdot V^2 + 0.2039 \cdot V - 0.0317$	0.91	1.0 - 3.0	116
GRF_{Prop}	$-0.0428 \cdot V^2 + 0.2420 \cdot V - 0.0378$	0.80	1.0 - 3.0	106
GRF_{v1}	$-0.2088 \cdot V^2 + 0.9147 \cdot V + 0.3241$	0.43	0.8 - 3.0	191
GRF_{v2}	$-0.0131 \cdot V^2 + 0.3032 \cdot V + 0.7545$	0.92	0.8 - 3.0	181

Table 3: Best fit regression equations for running gait parameters based on gait velocity, V ($m \cdot s^{-1}$). Velocity range and approximate number of subjects (N) are included.

	Regression Equation	R^2	V Range	N
Gait Timing				
SL (m)	$-0.0244 \cdot V^2 + 0.4612 \cdot V - 0.0451$	0.98	1 - 10.16	205
SR (steps/sec)	$0.0209 \cdot V^2 + 0.0081 \cdot V + 2.4663$	0.94	1 - 10.16	205
t_c (sec)	$0.5508 \cdot V^{-0.6531}$	0.87	1 - 9.5	215
Ground reaction forces (BW)				
GRF_{Brake}	$0.0943 \cdot V^{1.0759}$	0.73	1.5 - 6	240
GRF_{Prop}	$0.0781 \cdot e^{0.3805 \cdot V}$	0.83	1.5 - 6.25	203
GRF_{v1}	$0.8456 \cdot e^{0.2174 \cdot V}$	0.57	2.9 - 5.5	314
GRF_{v2}	$-0.0778 \cdot V^2 + 0.7695 \cdot V + 0.8679$	0.37	1.5 - 7	330

5.3 Future Work

Our planned work in the development of biomechanical regression relations will further improve our biomechanical description of physical training by (1) the expansion of our quantification to other movements (e.g., those done during obstacle course runs), and (2) the analysis variations in loading conditions between individual subjects for a given movement. However, the development of a better understanding of the entire regimen for the military, and more detailed descriptions of the various activities will need to be documented and categorized. We further recommend thorough documentation of any changes in the training protocol from the original plan. Further video analysis and GRF measurements may be needed to fully document some of the more complex exercises. Differences in loading conditions could then be correlated to individual measures such as anthropometry, medical history, or fitness level. These improvements should allow a more accurate quantification of the loading conditions experienced by an individual during the wide-ranging conditions experienced.

6. Key Research Accomplishments

We have:

1. Performed an in-depth review of the scientific literature regarding:
   a. the current status of bone overuse injury research, specifically in the areas of the mechanisms of injury;
   b. predictive fatigue and failure modeling;
   c. attempts at statistical risk factor analysis, as well as
   d. state-of-the-art and emerging diagnostic techniques.
2. Developed an anatomic biomechanical model which predicts temporally- and spatially- varying bone strains from laboratory tests using:
   a. inverse dynamics;
   b. nonlinear muscle force optimization, and
   c. detailed 3D FEM structural analysis.
3. Formulated regression equations which can infer gait timing and ground reaction force parameters from a simple description of the activity performed.

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7. Reportable Outcomes

Through our research we have shown:

1. A "stress fracture" is often not a frank fracture at all, but rather it is a pathological response of the body to an imposed fatigue strain in the bone.
2. An improvement in the fundamental understanding of how bones adapt and fail is needed before predictive modeling of bone overuse injuries will become accurate and reliable.
3. State-of-the-art technologies used to diagnose bone overuse injuries are time consuming, expensive and, for some, potentially dangerous.
4. Risk factor analysis based on demographics, personal history, anthropometrics and training errors is insufficient to gain true insight into the biological and biomechanical variations that discriminate those who are prone to bone overuse injury from those who are not.
5. When precise laboratory measurements of kinematics and ground reaction forces are available, biomechanical models—including inverse dynamic models, muscle load-sharing models, and finite element models of long bones—can provide a good estimation of skeletal strains.
6. Our modeling approach shows that muscle forces have a protective effect on the skeleton.
7. Regression equations can relate subjective descriptions of training performed to quantitative data pertaining to skeletal fatigue life prediction.

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8. Conclusions

8.1 Research Findings

Bone adapts both morphologically and microstructurally under repetitive loads through the biological processes of modeling and remodeling. Bone overuse injuries result from an imbalance between damage accumulation and repair. They are often caused by the increased physical demands of activities such as those involved in military boot camp training. The scientific community's fundamental understanding of how bones sense and adapt to new mechanical loads, from the level of bone cells to that of whole bones, remains incomplete; but it is widely accepted that an in depth knowledge of strains in the bone is quintessential to the accurate prediction of skeletal degradation and repair.

A "stress fracture" is not a frank fracture at all, but rather it is a pathological response of the body to an imposed fatigue strain in the bone. It is prevalently thought that the rate of bone adaptation is related to the damage present in the bone. Yet a growing number of researchers are coming to believe that other factors such as intraskeletal blood flow and oxygen deprivation of bone cells may in fact be the root stimuli for remodeling. Of the two most promising bone overuse injury prediction models, the Taylor model and the Martin model, neither is currently suitable to be employed as a quantitative predictive tool. The shortcomings of these models are largely due to insufficient data pertaining to the physical and biological processes governing bone damage and repair being available as well as the lack of good methods to gather such data. An improvement in the fundamental understanding of how bones adapt and fail is needed before predictive modeling will become accurate and reliable.

In the previous phase of the overuse injury assessment project, we developed a preliminary bone overuse injury prediction model based on the Taylor model and available field test data. However, the applicability of the model is severely limited by several factors. First, many of the model's biologically-based parameters cannot be accurately estimated using the data currently available in the literature. We have found that there is a lack of consensus within the scientific community even with regards to which biological processes are most significant in bone overuse injuries. Second, the stresses used in the preliminary model were based on nominal stress predictions. A progressive modeling approach needs to describe the temporally- and spatially-varying strain fields within load-bearing bones more completely than simple volume-averaged approximations. Finally, there is an unfilled gap between the data which is desired for biomechanical analysis and that which can be realistically provided from the field. We found that relations were needed which could convert the data acquired in the field, such as

a description of the training regimen, into useable scientific data such as ground reaction forces and loading rate.

We have also found that state-of-the-art technologies used to diagnose bone overuse injuries are time consuming, expensive and, for some, potentially dangerous. MRI is now the gold-standard for detecting bone overuse injuries, being entirely safe and having the greatest diagnostic power, but is also the most expensive technology. In contrast, some cheaper emerging technologies such as ultrasound are reviewed which are entirely safe, but have yet to be developed to a point where they are reliable indicators of a pathological bone condition.

Risk factor analysis is another commonly used method to determine which individuals and populations are most susceptible to bone injury. However, few such factors are widely recognized as being significant predictors of bone overuse injury. Conventional risk factor analysis based on demographics, personal history, anthropometrics and training errors is insufficient to gain real insight into the biological and biomechanical variations that separate those who are prone to bone overuse injury from those who are not. However, the approach we have taken to skeletal strain prediction—one which incorporates both biomechanics and structural mechanics—will be an indispensable tool for future and retrospective parametric evaluations of the significance of various risk factors.

A wide chasm exists between biomechanics research, which is used to determine joint and muscle forces on rigid bone segments during human locomotion, and the use of structural finite element modeling of individual bones to understand the strain fields the bone sees during typical loading. We have developed a three-dimensional musculoskeletal model which can predict skeletal strains using conventional laboratory measurements. The results of our model show that muscles have a protective effect on the skeleton and our findings corroborate with published findings of others.

When precise laboratory measurements of kinematics and ground reaction forces are available, biomechanical models—including inverse dynamic models, muscle load-sharing models, and finite element models of long bones—may be employed to provide an accurate estimation of bone strains as inputs to the models. However, when analyzing real-life training data, such laboratory measurements are not always available. For these cases, we have developed regression equations which are useful in relating subjective descriptions of the training performed to quantitative data pertaining to skeletal fatigue life prediction. Our current work in modeling laboratory-based data is integral to this latter effort.

8.2 Research Relevance

Each contribution in our continuing research on how human locomotion directly affects the spatially- and temporally-varying strain fields in load-bearing bones is another piece in the puzzle of how to detect and prevent bone overuse injuries. Specifically, our research can become a basis to compare different prospective training regimens by examining their potential for bone overuse injury. In-depth knowledge of skeletal fatigue strains resulting from different physical activities—information which has been unavailable to boot camp instructors in the past—will be the foundation for such a prediction. Once these skeletal loads are better understood, it is then possible to reasonably predict the bone overuse injury rate for a given training regimen. Such an approach will introduce a level of objectivity never before known in the comparison of prospective training regimens. We plan to continue refining our modeling approach to be more accurate and efficient. Every step forward in our research is taken with the needs of the end user in mind.

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Appendix

Timing and ground reaction force estimates for normal human walking and running at a variety of speeds: a survey of the literature

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Abstract

A survey of existing data was used to derive a set of velocity-based regression equations to predict the basic timing and ground reaction force (GRF) measures during human gait. Situations exist where acquiring timing and GRF data directly is not feasible, such as studies of large populations, and these equations may be beneficial. In addition, knowledge of the variability (or lack of variability) of these gait measures across a more general population may be of value, giving researchers an objective comparator for new biomechanics sensors and protocols. A literature survey was conducted where we sought key gait timing and GRF data for both running and walking. Variables included: step length, step rate, and foot contact time as well as peak braking, propulsive and vertical forces. From this data, velocity-based best-fit regression equations were calculated. Data was acquired based on values from approximately 763 subjects under speeds ranging from 0.25 to 3.0 m/s for walking and 571 subjects running at speeds from 1.0 to 10.9 m/s. Regression equations and data were plotted to allow researchers to easily compare the results to their own values. To maximize the utility of this analysis, we sought the largest sample size possible, employing a variety of different data collection methods and sample populations. We find that regressions for step length and step rate for both walking and running fit the observed data well but there is a lack of consensus for GRF's at higher speeds of walking and running.

Keywords: Regression equations; normative data; gait

Introduction

Ambulation is a primary function for our limbs and numerous studies have analyzed many aspects of gait to gain further insight into human movement. For example, gait analyses can reflect physiological changes due to training, injury, fatigue, disease, and age. In addition, changes in gait due to equipment such as footwear can aid in the evaluation and design of these products.

Currently accepted descriptors of gait include timing and force measurements using equipment that is now common in most biomechanic laboratories. Timing measures include step length (*SL*), step rate (*SR*) and the foot contact time (t_c). With the development of force platforms and in-shoe pressure sensing devices, measurement of ground reaction forces (GRF's) has also become common. Because GRF's are complex patterns that vary with time, peak values are often identified for analysis and reported in the literature. In general, *SL* and GRF peak values increase while *SR* and t_c decrease with speed for both running and walking. A plethora of studies have measured gait timing and GRF variables confirming this trend under many situations and typical values for both running and walking can be found in most biomechanics textbooks (Winter, 1990).

Despite the relative ease of collecting both timing and GRF values for human walking and running, there are several situations where acquiring this type of data is not feasible and using a velocity-based regression equation may be a viable alternative. For example, estimating gait parameters for large populations is impractical, such as with military recruits undergoing basic training, and simple measures like distance to predict fitness and injury have been used with mixed results (Trank et al., 2001; Popovich et al., 2000). A more accurate quantification of training intensity using regression-based gait parameters may lead to better results. Regressions can also be used if runways are too short and only allow data to be collected on a single step at the desired speed. In addition, regression equations give a point of reference for GRF sensor calibrations and can aid in the selection of reasonable input values for mathematical gait models. And finally, the equations can help editors, allowing them to quickly verify that data falls within a reasonable range, potentially catching errors prior to publication.

A review of the literature reveals that several researchers have published velocity-based regressions for both timing and GRF variables. Previous to 1970, most regressions focused on timing variables for walking, most notably stride rate (Grieve and Gear, 1966; Workman and

Armstrong, 1966; Dean, 1965). Around 1990, timing variables for walking was revisited and regressions developed for people of Japanese descent (Yamasaki et al., 1991; Hirokawa and Matsumara, 1987). Interestingly, it was not until 1996 that simple velocity-based linear regressions for walking and running GRF's were published (Breit and Whalen, 1997; Keller et al., 1996) despite the wide use of force platforms. No velocity-based regressions were found for running *SL*, *SR*, and t_c.

Some of the problems with the currently published regression equations are that the references may be difficult to acquire (pre-1970), the values are normalized to other potentially missing parameters such as age and height (Samson et al., 2001; Stolze et al., 2000), and the equations are limited in scope by the number of test subjects and range of speeds (Yamasaki et al., 1991). Thus, there is a need for a set of regression equations to estimate common gait parameters covering a variety of velocities where direct measurement of these values may not be possible.

We chose to address this issue by surveying published results to acquire average values for both gait timing and GRF's over a wide range of speeds, effectively utilizing the results from a larger number of subjects and speeds than would be practical for a single laboratory to acquire. In addition, this analysis will give a better appreciation of the variability (or lack of variability) of some of these gait measures across the general population as well as identify speeds where basic gait parameter measures are missing from publication.

Methods

The literature survey was conducted primarily using PubMed, an online medical journal database, to acquire original research articles where gait timing or GRF's were collected for both running and walking. For the survey, we assumed researchers used the typical definition of walking and running—as gait with a dual support phase and gait with an airborne phase, respectively. To keep the results as general as possible, only subjects of adult age (mean age approximately 27 yrs, range: 15-70 yrs) using freely chosen step rates and step lengths were incorporated. Subjects carrying additional loads (or negative loads) were not included. In addition, both male and female genders were combined and no distinction was made for athletic ability, footwear (barefoot, boots, athletic shoes, etc.), or gait surface (treadmill or overground). To be included in this survey it was required that mean gait speed, V ($m \cdot s^{-1}$) be reported. Average rather than individual gait parameter values were used.

Timing variables gathered include step rate, step length, and time of foot contact. Step rate (SR) is defined as the number of left and right steps per second, i.e., there are two steps per stride. Step length (SL) is the distance in meters between left and right steps, i.e., half the length of a stride. If average gait velocity was available but either average SR or SL was not reported, the following definition was used to determine the missing value:

$$V = SL \times SR \quad (1)$$

where V ($m \cdot s^{-1}$) is the average gait velocity. Foot contact time (t_c), often referred to as stance time for walking, was defined as the time in seconds that one foot is in contact with the ground during a stride.

GRF's acquired for this study include average peaks from the vertical and anterior-posterior directions, normalized to body mass. For walking, GRF_{V1} and GRF_{V2} are the braking and propulsive phase vertical components, respectively. For running, GRF_{V1} is shorter in duration and is often referred to as the impact peak whereas GRF_{V2} is the longer thrust phase. In the anterior-posterior direction, GRF_{Brake} is the braking and GRF_{Prop} is the propulsive peak forces for both running and walking.

Each study's average gait parameter value reported was plotted versus the average velocity. Linear, logarithmic, polynomial, power, and exponential forms of the regression equation were tested and the equation with the best-fit, as determined by the greatest R^2 value, was noted. Previously published equations, whose regressions were derived from gait velocity, were compared to this study's results.

Results

Seventy-three journal articles were selected for inclusion in this review with most articles reporting on gait timing measures (82%). Thirty-three papers were found with peak GRF values for both running and/or walking. Data was acquired based on values from approximately 763 subjects under speeds ranging from 0.25 to 3.0 m/s for walking and 571 subjects running at speeds from 1.0 to 10.9 m/s. We acknowledge that it is not feasible to include every known publication of human gait.

Figure 12 shows timing and GRF variables versus walking speed overlaid with the best fit regression and, when available, any previously published regressions. Figure 13 depicts the

same results for running. The best fit regression equations, velocity range, and reference source for each gait parameter can be found in Table 4 and Table 5. For walking, *SR*, *SL*, GRF_{V2}, GRF_{Brake} and GRF_{Prop} regression equations fit the data well ($R^2 > 0.80$) while the t_c and GRF_{V1} equation fit was not as good ($R^2 \leq 0.60$). For running, high goodness-of-fit was seen for all of the gait timing measures and GRF_{Prop} ($R^2 > 0.80$). The remaining running GRF equations had R^2-values of less than 0.75.

Discussion

Our literature review found a large number of average values for common gait parameters covering a range of speeds for normal adult walking and running. In addition, the regression equations developed from this data appear to reasonably reproduce estimates of the gait parameters and, in most cases, are in agreement with previously published equations while covering a wider range of velocities.

We acknowledge that our results presume that the original data was collected and reported accurately as well as similarly and that other factors such as gender and footwear may be altering our results. For example, filtering high frequency noise is common for GRF signals. However, various levels of filtering will attenuate peak values and are likely responsible for some of the wide variation in reported values seen for the running impact peak, GRF_{V1}. In addition, the accuracy of t_c is dependent on the sensitivity of the measurement device and some of the variability we observe may be due to differences in the threshold sensitivity of the foot contact sensors. Also, there may be changes in gait parameters due to factors such as footwear (Hamill and Bensel, 1996; De Wit et al., 2000; Clarke et al., 1983; Komi et al., 1987; Milani et al., 1997; Cavanagh and Williams, 1979; Nigg and Morlock, 1987), and gender (Hangland and Cimbalo, 1997; Yamasaki et al., 1991; Keller et al., 1996). However, data from all subjects, regardless of the experimental arrangement, were included when possible and the widest range of situations is represented by our data. Thus, the values shown in Figure 12 and Figure 13 as well as the regression equations in Table 4 and Table 5 are representative of values that can be expected from situations commonly found in a gait analysis.

As shown in Equation 1, the relationship between *V*, *SR* and *SL* is well established (Zatsiorky et al., 1994) and our results continue to supports this. We note that the equations derived (Table 4 and Table 5) try to maintain the functional form of Equation 1 even though this "constraint" was not required of the regressions. Small differences seen in the *SR* and *SL*

relationships are likely due to round off and experimental biases. For example, Stolze et al. (2000) measured *SL* and *V* on different parts of the runway where velocities could differ slightly. Also, the "±5% target velocity" reported by Komi et al. (1987) is not necessarily the average *V* we seek.

Graphical representation of the results (Figure 12 and Figure 13) are included as a visual aid for researchers. These graphs should allow comparisons of any new data to this collection of previously published findings quickly and easily. In addition, the range of variability and number of values obtained for a given speed can be determined visually, something that cannot be ascertained from the regression equations alone. Note that we were unable to incorporate the data that Briet and Whalen (1997) used for their regressions as average values over the range of speeds and subjects tested was not given.

The equations developed in this study are in agreement with most of the previously published regressions but with the added advantage of covering a wider range of velocities and utilizing a larger number of subjects. As reviewed by Zatsiorky et al. (1994), some of the earliest published walking regressions found that both *SL* and *SR* are proportional to $V^{0.5}$ and our results continue to support this finding. In addition, for running *SR*, *SL*, t_c, and GRF_{V1} we introduce velocity-based regressions that, to our knowledge, have not been published. Unfortunately, we were unable to compare our results with the equations published by Samson et al. (2001) or Stolze et al. (2000), which were height- and age- rather than velocity-based.

Our review indicates that few studies report peak GRF's and that there is a lack of consensus for GRF's at higher speeds of walking and running. See Figure 12 and Figure 13. While many experiments collect and utilize force platform data to calculate joint moments, often only the resultant moments (Kerrigan et al., 1998) or energetics (Hangland and Cimbalo, 1997) are described. In addition, those studies that published GRF's (both data and regressions) often utilize a limited number of subjects (Dufek et al., 1990) or speeds (Crossley et al., 1999). Also, running and walking form at high speeds may be dependent on factors such as running style (Keller et al., 1996) and fatigue level (Christina et al., 2001). Thus, it is difficult to determine whether the wide variability seen in GRF's at higher speeds is characteristic of normal gait. We believe that more measurements at higher speeds will help researchers determine whether their own results are typical or are being affected by other factors. Thus, this review highlights the

need for more GRF data to be published in the literature despite the wide spread use these values.

To maximize the utility of this analysis, we sought the largest sample size possible, employing a variety of different data collection methods and sample populations. We gratefully acknowledge that this paper results from the effort of a large number of people encompassing almost 40 years of independent research. We strove to make the values and equations reported here representative of the general adult population by combining their cumulative results.

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Table 4. Best fit regression equations for walking gait parameters based on gait velocity, V ($m \cdot s^{-1}$). Velocity range and approximate number of subjects (N) are included.

	Regression Equation	R^2	V Range	N	Source
Gait Timing					
SL (m)	$0.6230 \cdot V^{0.4812}$	0.86	0.25 - 3.0	655	A, B
SR (steps/sec)	$1.6062 \cdot V^{0.5175}$	0.88	0.25 - 3.0	655	A, B
t_c (sec)	$-0.3794 \cdot \mathrm{Ln}(V) + 0.7607$	0.60	0.5 - 3.0	318	A, C
Ground reaction forces (BW)					
GRF_{Brake}	$-0.0259 \cdot V^2 + 0.2039 \cdot V - 0.0317$	0.91	1.0 - 3.0	116	D, E
GRF_{Prop}	$-0.0428 \cdot V^2 + 0.2420 \cdot V - 0.0378$	0.80	1.0 - 3.0	106	D
GRF_{v1}	$-0.2088 \cdot V^2 + 0.9147 \cdot V + 0.3241$	0.43	0.8 - 3.0	191	D, E, F, G
GRF_{v2}	$-0.0131 \cdot V^2 + 0.3032 \cdot V + 0.7545$	0.92	0.8 - 3.0	181	D, F

A (Nilsson and Thorstensson, 1989; Martin and Marsh, 1992; Murray et al., 1970; Yamasaki et al., 1991; Borghese et al., 1996; Chao et al., 1983; Jansen et al., 1982; Martin and Nelson, 1986; Lemke et al., 2000; Mills and Barrett, 2001; Stolze et al., 1997; Stolze et al., 1998; Nilsson et al., 1985; Kinoshita, 1985; Rosenrot et al., 1980; Mann and Hagy, 1980)

B (Blanke and Hageman, 1989; Burdett et al., 1983; Cotes and Meade, 1960; Cunningham et al., 1982; Donelan and Kram, 1997; Goh et al., 1998; Griffin et al., 2003; Hageman and Blanke, 1986; Hangland and Cimbalo, 1997; Himann et al., 1988; Kerrigan et al., 1998; Minetti et al., 1994b; Minetti et al., 1995; Powers et al., 1999; Stolze et al., 2000; Wearing et al., 2000; White et al., 1998; Willson et al., 2001)

C (Hamill et al., 1984; McCrory et al., 2001)

D (Nilsson and Thorstensson, 1989; Martin and Marsh, 1992; Hamill and Bensel, 1996; Borghese et al., 1996; Simpson and Jiang, 1999; Himann et al., 1988; Kinoshita, 1985)

E (Cavanagh and Williams, 1979)

F (Dufek et al., 1990; Hamill et al., 1984; McCrory et al., 2001; White et al., 1998)

G (Powers et al., 1999)

Table 5. Best fit regression equations for running gait parameters based on gait velocity, V ($m \cdot s^{-1}$). Velocity range and approximate number of subjects (N) are included.

	Regression Equation	R^2	V Range	N	Source
Gait Timing					
SL (m)	$-0.0244 \cdot V^2 + 0.4612 \cdot V - 0.0451$	0.98	1 - 10.16	205	A, B
SR (steps/sec)	$0.0209 \cdot V^2 + 0.0081 \cdot V + 2.4663$	0.94	1 - 10.16	205	A, B
t_c (sec)	$0.5508 \cdot V^{0.6531}$	0.87	1 - 9.5	215	A, C
Ground reaction forces (BW)					
GRF_{Brake}	$0.0943 \cdot V^{1.0759}$	0.73	1.5 - 6	240	D, E
GRF_{Prop}	$0.0781 \cdot e^{0.3805 \cdot V}$	0.83	1.5 - 6.25	203	D, F
GRF_{v1}	$0.8456 \cdot e^{0.2174 \cdot V}$	0.57	2.9 - 5.5	314	G, H
GRF_{v2}	$-0.0778 \cdot V^2 + 0.7695 \cdot V + 0.8679$	0.37	1.5 - 7	330	G, I

A (Chang and Kram, 1999; Chang et al., 2000; De Wit et al., 2000; Kyrolainen et al., 2001; Mann and Hagy, 1980; Minetti et al., 1994a; Munro et al., 1987; Wright and Weyand, 2001)

B (Brisswalter et al., 1996; Bus, 2003; Cavanagh and Kram, 1989; Craib et al., 1994; Komi et al., 1987; Mercer et al., 2002; Mero and Komi, 1986; Svedenhag and Sjodin, 1994; Wank et al., 1998)

C (Arampatzis et al., 2000; Clarke et al., 1983; Farley and McMahon, 1992; Frederick and Hagy, 1986; Freychat et al., 1996; Hamill et al., 1984; Mann and Sprague, 1980; Nilsson and Thorstensson, 1989; Roberts et al., 1998; Williams et al., 1987; Nilsson et al., 1985)

D (Chang and Kram, 1999; Chang et al., 2000; Nilsson and Thorstensson, 1989; Cavanagh and Lafortune, 1980; Hamill and Bensel, 1996; Williams et al., 1987; Nachbauer and Nigg, 1992; Feehery, Jr., 1986; Freychat et al., 1996; Bus, 2003)

E (Crossley et al., 1999)

F (Kyrolainen et al., 2001)

G (Crossley et al., 1999; Hamill et al., 1984; Cavanagh and Lafortune, 1980; Munro et al., 1987; Martin and Marsh, 1992; Hamill and Bensel, 1996; Clarke et al., 1983; Williams et al., 1987; Nachbauer and Nigg, 1992; Feehery, Jr., 1986; Christina et al., 2001; Freychat et al., 1996; Frederick and Hagy, 1986; Bus, 2003; Dufek et al., 1990)

H (Dixon et al., 2000; Komi et al., 1987; Milani et al., 1997; Nigg and Morlock, 1987)

I (Chang and Kram, 1999; Chang et al., 2000; Keller et al., 1996; Kyrolainen et al., 2001; Nilsson and Thorstensson, 1989)

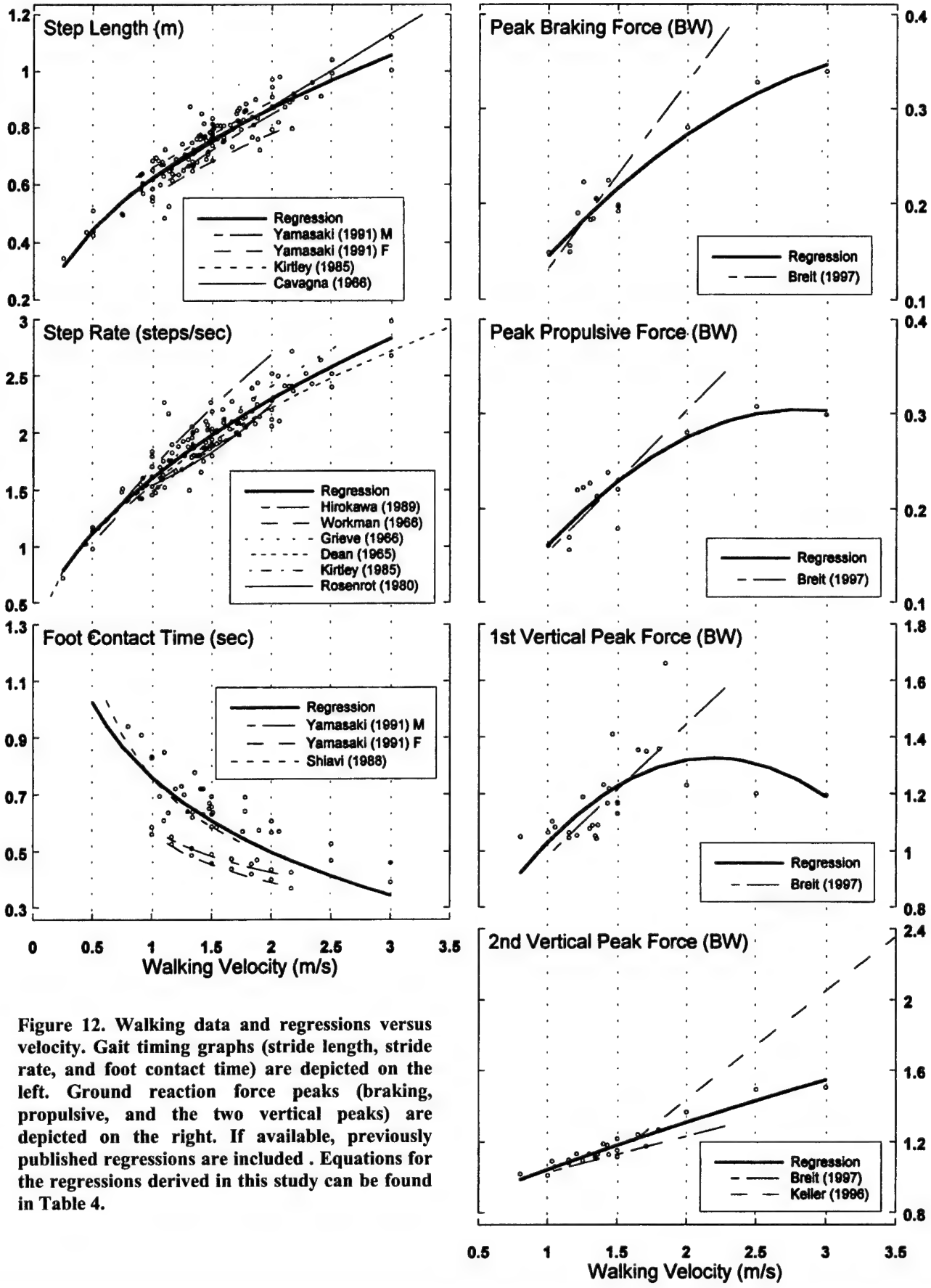

Figure 12. Walking data and regressions versus velocity. Gait timing graphs (stride length, stride rate, and foot contact time) are depicted on the left. Ground reaction force peaks (braking, propulsive, and the two vertical peaks) are depicted on the right. If available, previously published regressions are included . Equations for the regressions derived in this study can be found in Table 4.

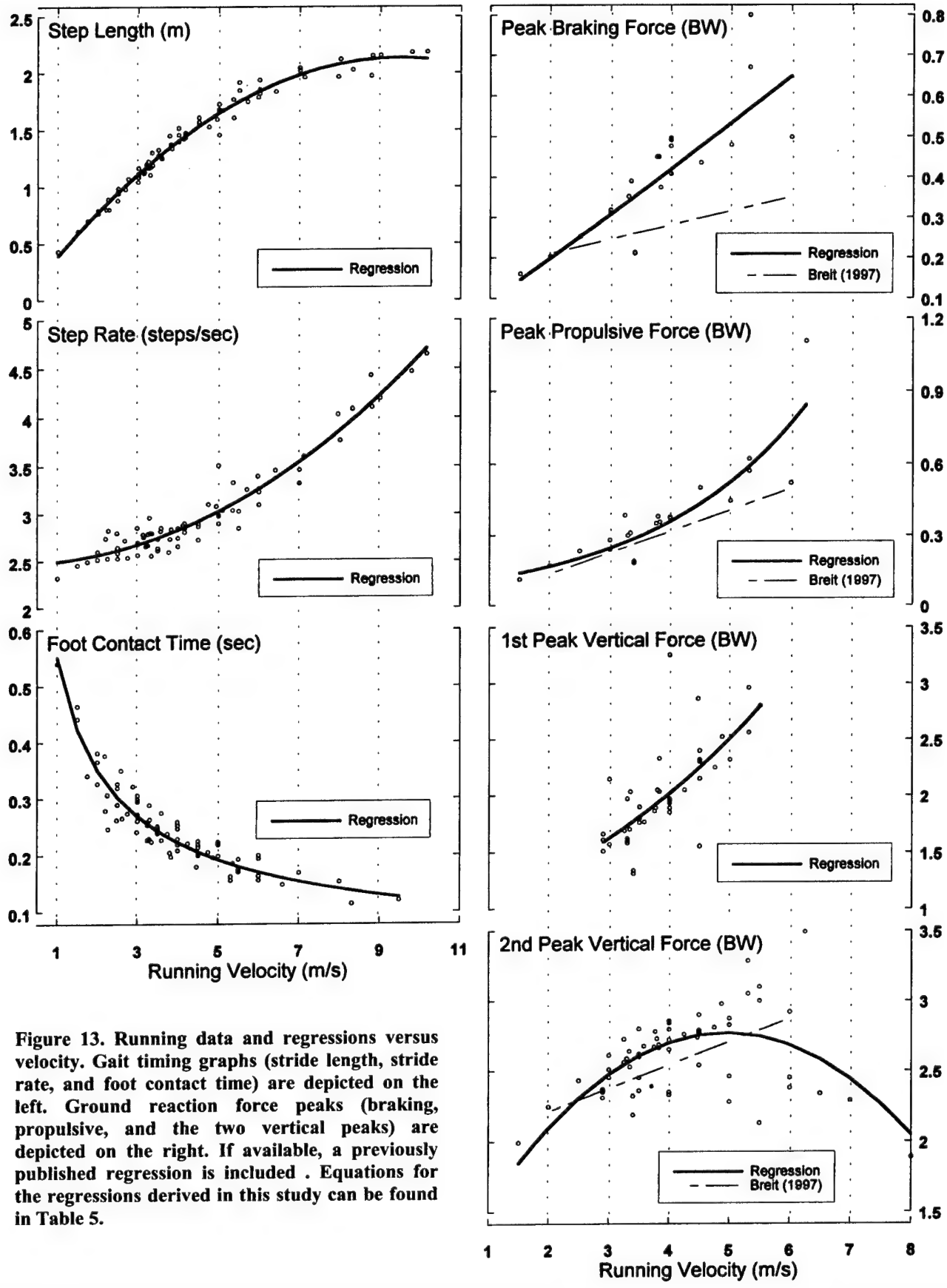

Figure 13. Running data and regressions versus velocity. Gait timing graphs (stride length, stride rate, and foot contact time) are depicted on the left. Ground reaction force peaks (braking, propulsive, and the two vertical peaks) are depicted on the right. If available, a previously published regression is included . Equations for the regressions derived in this study can be found in Table 5.

Table and Figure Captions

Table 4. Best fit regression equations for walking gait parameters based on gait velocity, V ($m \cdot s^{-1}$). Velocity range and approximate number of subjects (N) are included.

Table 5. Best fit regression equations for running gait parameters based on gait velocity, V ($m \cdot s^{-1}$). Velocity range and approximate number of subjects (N) are included.

Figure 12. Walking data and regressions versus velocity. Gait timing graphs (stride length, stride rate, and foot contact time) are depicted on the left. Ground reaction force peaks (braking, propulsive, and the two vertical peaks) are depicted on the right. If available, previously published regressions are included . Equations for the regressions derived in this study can be found in Table 4.

Figure 13. Running data and regressions versus velocity. Gait timing graphs (stride length, stride rate, and foot contact time) are depicted on the left. Ground reaction force peaks (braking, propulsive, and the two vertical peaks) are depicted on the right. If available, a previously published regression is included . Equations for the regressions derived in this study can be found in Table 5.

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